Estimating HIV prevalence in the general female population in Great Britain using data from pregnant women ~~having live births~~

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Abstract

Globally HIV is increasing rapidly amongst women and an appreciation of the total burden of infection amongst this population group is essential for planning purposes. In GB women having live births are taken to be representative of all women. Monitoring is undertaken using samples from neonates as maternal antibodies to HIV cross the placenta prior birth. However, results may be biased as pregnant women could differ from all women in terms of HIV prevalence and those with HIV could have differential fertility than uninfected women. In this thesis, ways to improve the extrapolation of neonatal seroprevalence to all women are investigated.

The application of pregnant women data to all women assumes no differential fertility between persons at varying risk of HIV infection. However, analyses showed African women have both higher HIV and fertility rates than other women. In addition, results from a literature review suggested that HIV infected women may have reduced live birth rates after diagnosis, although it was unclear whether recent advances in the therapeutic and mother to child prophylactic management for HIV infected women have affected women's desire for children. A cross-sectional questionnaire study carried out to address these questions showed a third of HIV positive women did not want children after they received their HIV diagnosis. Of this group, approximately half changed their desire for children due to improvements in HIV management. Additional analyses confirmed recent changes in childbearing patterns amongst HIV positive women were likely to have taken place and that the factor most strongly associated with desire for children was reproductive history.

A model developed using results described above estimated 16,000 women were living with HIV in GB in 2002. This was more than previously estimated using a 'direct' approach, reflecting an improved methodology accounting for differences in fertility and HIV risk between pregnant and non-pregnant women.

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List of Abbreviations

AIDS	Acquired immuno-deficiency syndrome
ANC	Antenatal clinic attenders
CDSC	Communicable Disease Surveillance Centre
DBS	Dried Blood Spot
ECS	European Collaborative Study
GB	Great Britain
GRO	General Register Office
HAART	Highly active anti-retroviral therapy
HIV	Human immuno-deficiency virus
HPA	Health protection Agency
ICH	Institute of Child Health
IDU	Injecting drug user
MTCT	Mother to child transmission
NATSAL	National Study of Sexual Attitudes and Lifestyles
NSHPC	National Study of HIV in Pregnancy and Childhood
ONS	Office for National Statistics
RIR	Relative Inclusion Ratio
SCIEH	Scottish Centre for Infection and Environmental Health
SOPHID	National Survey of Prevalent HIV Infections Diagnosed
SSA	Sub-Saharan Africa
STI	Sexually Transmitted Infection
TOP	Termination of pregnancy
UA	Unlinked Anonymous
UNAIDS	United Nations Programme on HIV/AIDS
WHO	World Health Organisation

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Chapter 1: Demography patterns and HIV risk amongst women in Great Britain

1.1: Introduction

Now in its third decade, the human immuno-deficiency virus (HIV) / acquired immuno-deficiency syndrome (AIDS) pandemic has been disastrous from a public health perspective. The Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organisation (WHO) estimated that globally by the end of 2003 there were nearly 38 million adults and children living with HIV/AIDS (1). During 2003 almost 5 million people were newly infected with HIV, the greatest number in any given year since the beginning of the epidemic. In the same year almost 3 million people died from an AIDS-related death. Heterosexual transmission of HIV is the predominant exposure amongst adults, while mother-to-child transmission accounts for the majority of infections in children. The region of the world most affected by HIV is sub-Saharan Africa[1] (SSA) where over two thirds of the estimated numbers of infected people live. Globally, HIV infection in women accounts for nearly 50% of adult infections (1).

Accurate HIV prevalence estimates are needed to respond to the enormous challenge posed by HIV. The levels and associated risks for HIV infection require monitoring, both in adults whose risk behaviour makes them more at risk to infection (for example homo/bisexual men) and among the less at risk who are more broadly representative of the adult population (for example pregnant women) (2). These estimates are needed in order to detect changes in transmission patterns where HIV is already present and to recognise emerging problems elsewhere (3). In Great Britain (GB), estimates of

[1] Sub-Saharan Africa consists of Eastern Africa, Middle Africa, Southern Africa and Western Africa

HIV in the general adult population have been based on results from neonatal seroprevalence surveys (4-5). HIV prevalence amongst neonates reflects level of HIV infection amongst pregnant women as maternal antibodies pass over the placenta prior to birth (6). However, these results are potentially biased when estimating HIV amongst all women as only women who become pregnant and have a live birth will be included in neonatal surveys and these women may differ from others in terms of HIV prevalence (7).

The aim of this thesis was to investigate ways to improve the extrapolation of neonatal seroprevalence data to the general female population in GB, accounting among other factors for biases relating to the fertility differential between HIV-positive and HIV-negative women. As GB is a culturally diverse country with continuing waves of immigration, often from areas of high HIV prevalence rates such as Africa, and patterns of fertility and HIV prevalence are associated with the demographic characteristics of the population under study, chapter 1 begins with a brief description of the British population. Throughout the thesis many different sources of health information were used to address the overall aim of improving HIV prevalence estimates among the general population. These sources of information were collected according to different geographical areas. Therefore to aid interpretation of results, a brief description of the current organisation of health boundaries is given. Next a detailed description of HIV prevalence amongst women in GB is provided and the importance of monitoring HIV prevalence and the underlying assumptions when this is achieved through the use of neonatal seroprevalence data is discussed. Finally, techniques which have already been developed to adjust HIV prevalence estimates from pregnant women to be representative of HIV prevalence among all women of reproductive age are described, and areas for improvement identified.

1.2: Population of Great Britain

Great Britain[2] is situated in Northern Europe and is part of the European Union. As well as having close links with other countries within Europe, close ties exist with the Commonwealth[3]. Within GB is a universal health care system structured into geographic health boundaries, which over the last 10 years have changed a number of times. Figure 1.1 shows the organisation of the National Health Service for the 3 countries of GB. In England there have been major re-organisations in 1996, 2002 and 2003 and the current structure consists of 28 Strategic Health Authorities, which are constituted from groupings of the 303 Primary Care Organisations. Scotland has 15 Health Boards which form a single local health care system and Wales consists of 22 Local Health Boards (http://www.statistics.gov.uk/geography/health_geog.asp (accessed August 2004)). Infectious disease surveillance of HIV/AIDS is primarily organised on a national level by the Communicable Disease Surveillance Centre (CDSC) (England and Wales) and the Scottish Centre for Infection and Environmental Health (SCIEH) (Scotland).

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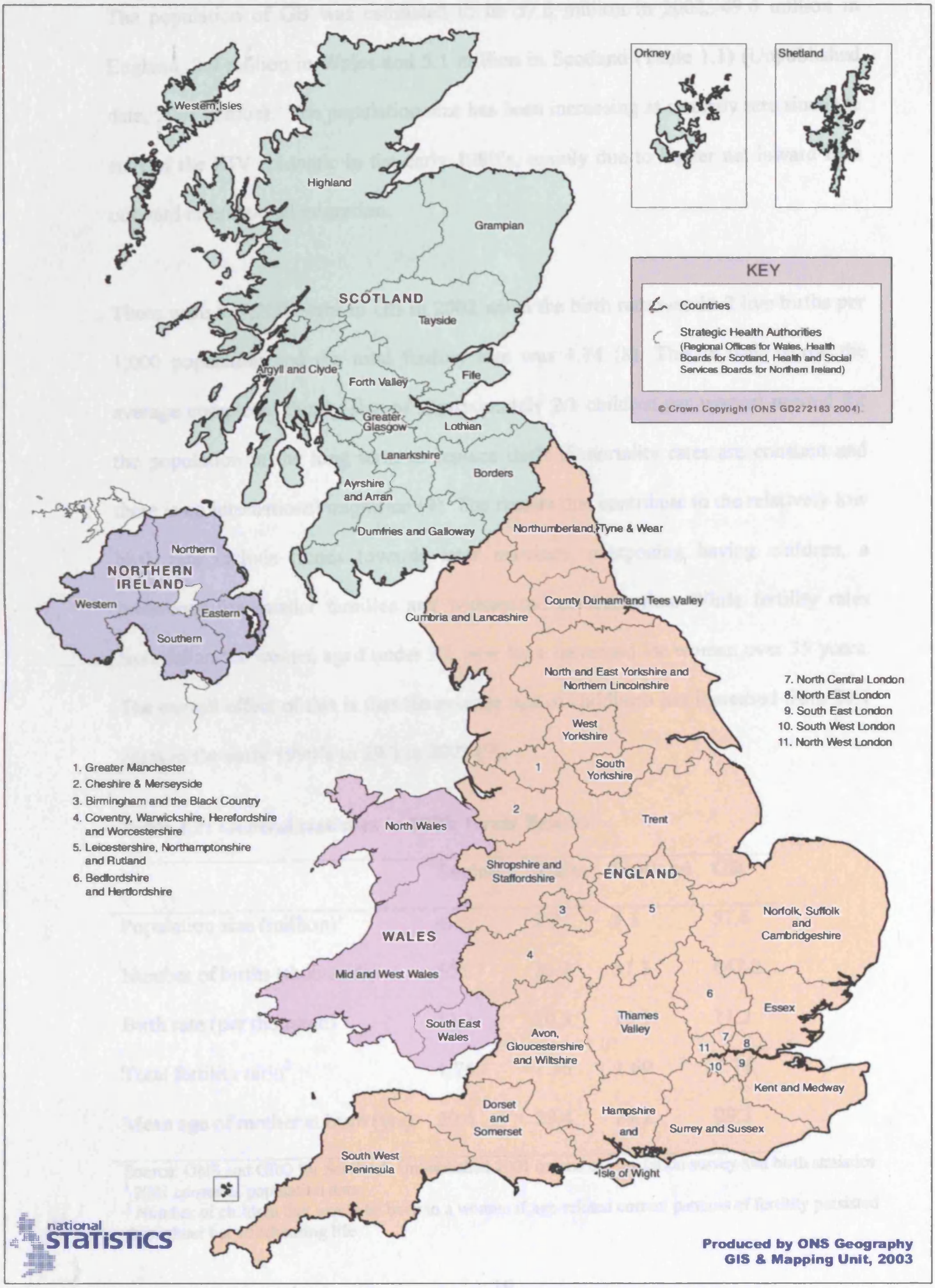
[2] Great Britain (GB) consists of England, Wales and Scotland and is part of the United Kingdom of Great Britain and Northern Ireland (UK).

[3] The old Commonwealth comprises Australia, Canada, South Africa and New Zealand; the New Commonwealth comprises of the other 49 sovereign states within the Commonwealth, including much of Africa, south Asia and the Caribbean

United Kingdom: Health Geography, 1 July 2003 to 8 February 2004



The population of GB was estimated to be 57.6 million in 2002, 49.6 million in England, 2.9 million in Wales and 5.1 million in Scotland (Table 1.1) (Unpublished data, 2001 census). The population size has been increasing at a steady rate since the start of the HIV epidemic in the early 1980's, mainly due to higher net inward than outward international migration.

There were 647,200 births in GB in 2002 when the birth rate was 11.2 live births per 1,000 population and the total fertility rate was 1.74 (8). This is well below the average completed family size of approximately 2.1 children per woman needed for the population in the long term to replace itself if mortality rates are constant and there is no international migration (9). The factors that contribute to the relatively low birth rate include trends towards later marriage, postponing having children, a preference for smaller families and widespread contraception. While fertility rates have fallen for women aged under 30, they have increased for women over 35 years. The overall effect of this is that the average age of childbirth has increased from 26.1 years in the early 1990's to 29.3 in 2002 (9).

Table 1.1: General statistics in 2002: Great Britain

	England	Wales	Scotland	GB
Population size (million)[1]	49.6	2.9	5.1	57.6
Number of births (thousands)	565.7	30.2	51.3	647.2
Birth rate (per thousand)	11.3	10.3	10.1	11.2
Total fertility ratio[2]	1.75	1.75	1.60	1.74
Mean age of mother at birth (yrs)	29.4	28.4	29.2	29.3

Source: ONS and GRO for Scotland. Unpublished 2001 census of population survey and birth statistics
[1] 2001 census of population data
[2] Number of children that would be born to a woman if age-related current patterns of fertility persisted throughout her childbearing life

1.2.1: Size and characteristics of the ethnic minority population in GB

Overall, according to the 2001 census, the total ethnic minority population in GB was estimated to be 4.6 million, 8.1% of the total population (Unpublished data 2001 census). These figures compare to 3.1 million or 5.5% of the total population in 1991 (10). Table 1.2 shows that of the individual ethnic minority groups, the south Asian population is most numerous followed by black Caribbeans and black Africans. Ninety five percent of the ethnic minority population live in England, and the majority of these are concentrated in large urban areas such as London where they comprise 28% of all residents. Three quarters of black Africans and half of Bangladeshis live in London whilst other minority ethnic groups are more dispersed throughout GB (10).

Table 1.2: Ethnic minority populations in Great Britain, 2001 Census data

	England	Wales	Scotland	GB
White	44,679,361 (90.9%)	2,841,505 (97.9%)	4,960,334 (97.9%)	52,481,200 (91.9%)
Mixed	643,373 (1.3%)	17,661 (0.6%)	12,764 (0.3%)	673,798 (1.2%)
South Asian	2,010,479 (4.1%)	21,984 (0.8%)	48,811 (1.0%)	2,081,274 (3.6%)
Black Caribbean	561,246 (1.1%)	2,597 (0.1%)	1,778 (0.04%)	565,621 (1.0%)
Black African	475,938 (1.0%)	3,727 (0.1%)	5,118 (0.1%)	484,783 (0.8%)
Black Other	95,324 (0.2%)	745 (0.03%)	1,129 (0.02%)	97,198 (0.2%)
Rest	673,110 (1.4%)	14,866 (0.5%)	32,077 (0.6%)	720,053 (1.3%)
All ethnic minority population (% total population)	*4,459,470 (9.1%)*	*61,580 (2.1%)*	*101,677 (2.0%)*	*4,622,727 (8.1%)*
All Population	**49,138,831**	**2,903,085**	**5,062,011**	**57,103,927**

Source: Unpublished Census 2001 population survey

There has been considerable variation in the absolute change in the numbers of people in each ethnic minority group, the largest rate of change occurring in the three black ethnic groups. Between the early and late 1990's the black African population increased by 37%. Over the same time period there was little change in the number of people identified as black Caribbean but a doubling of the number of individuals who were classified as black Other. Many individuals of black Caribbean origin classify themselves as black British as they had been born in GB. It is therefore difficult to make definitive statements about the characteristics of the population of black Caribbean origin (10).

The proportion of each ethnic group born in GB has been influenced by the timing of the various waves of immigration into this country as migrants are mainly young adults. Virtually all persons (97%) aged over 44 years from all ethnic groups were born outside the UK. In contrast, 90% of ethnic minority children aged under 15 years were born in the UK. There are considerable differences between the various ethnic minority groups, ranging from 25% of Chinese persons born in the UK to 89% of the black Other population (10). Of the 479,665 persons in England and Wales describing themselves as black African, 34% were born in the UK, 16% in Nigeria and 19% in other Central and West Africa (Table 1.3). In addition, a high proportion (24%) were born in South and East Africa and 1% were born in Asia. More persons were classified as born in SSA (740,266) than as black African (479,665) (Unpublished census 2001 data). This is because whilst the majority of persons born in Nigeria were black African, many persons born in Kenya, South Africa, Zimbabwe and other South and East Africa were either White or Indian (Table 1.4). The association between country of birth and ethnicity is of particular interest to this thesis as some of the key data sources used in analyses can only be presented according to country of birth of the woman rather than by ethnicity.

Table 1.3: Population of England and Wales describing themselves as Black Africans

Country of birth	Black African population	
	N	%
UK	162,330	34
Nigeria	76,291	16
Other Central and West Africa	89,980	19
Kenya	13,421	3
South Africa	4,218	1
Zimbabwe	17,852	4
Other South and East Africa	88,757	18
Asia	2,260	1
Other	24,556	5
TOTAL	**479,665**	**100**

Adapted from Table S102. Census 2001. CD supplement to the National report for England and Wales. Unpublished data. Office of National Statistics

Table 1.4: Percentage of people by country of birth in each ethic group

Country of birth	Total N	Ethnic Group							
		White N (%)		Black African N (%)		Indian N (%)		Other N (%)	
Nigeria	86,958	5,895	(7)	76,291	(87)	295	(1)	4,477	(5)
Kenya	127,322	16,565	(13)	13,421	(11)	82,727	(65)	14,609	(11)
South Africa	132,301	119,129	(90)	4,218	(3)	3,622	(3)	5,332	(4)
Zimbabwe	47,158	24,664	(52)	17,852	(38)	1,081	(2)	3,561	(8)
Other S and E Africa	235,884	31,606	(13)	88,757	(38)	73,173	(31)	42,348	(18)
Rest SSA	110,603	7,251	(7)	89,980	(81)	6,119	(6)	7,253	(6)
Total SSA	**740,226**	**205,110**	**(28)**	**290,519**	**(39)**	**167,017**	**(23)**	**77,580**	**(10)**

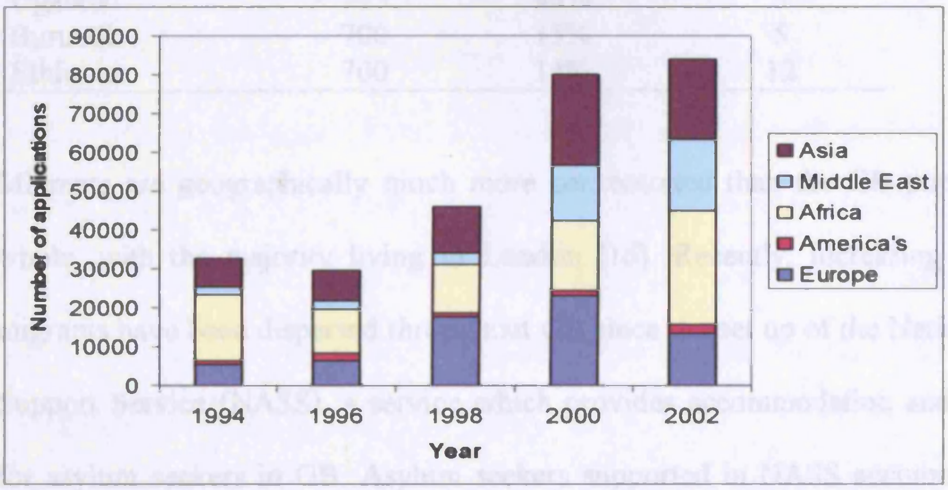
Adapted from Table S102. Census 2001. CD supplement to the National report for England and Wales. Unpublished data. Office of National Statistics

The age structure of the ethnic minority groups is also influenced by age at migration and differential fertility rates between the various groups. Women born in developing countries tend to have higher fertility rates than women born in the UK. For example total fertility rates for countries in SSA range from 4.1 in Zimbabwe to 4.7 in Kenya and 7.0 in Uganda (11). However, fertility in non-UK born women tends to fall gradually with the passage of time following immigration (12).

1.2.2: International Migration

Migration to and from countries outside of GB is currently a major component of population change (13). Almost a third of the total migrant population living in GB arrived during the last decade, reflecting the increases in migration over this period (Figure 1.2). Numbers of applications have increased from all parts of the world, often from where there is war or conflict (14), with the most notable increases from Africa, Eastern Europe and the Middle East. Whilst the source countries from which migrants come are diverse, the current stock of migrants still reflects significant immigration waves from the Caribbean, Pakistan and Bangladesh which occurred in the 1960s and 70s.

Figure 1.2: Numbers of applications received for asylum in the UK, excluding dependents by world region 1994-2002



Source: Home Office. Asylum Statistics. 3rd Quarter 2003. United Kingdom 2004

In 2002 the highest number of applications were from nationals of Iraq (14,570), Zimbabwe (7,655), Afghanistan (7,205), Somalia (6,540) and China (3,675) (13). A consistently high number of applications are received from SSA, an area of the world with high HIV prevalence rates. Approximately half of all applications from Africa in 2002 were from either Zimbabwe or Somalia (Table 1.5). Compared with 2001, large increases occurred most notably in the number of applications from nationals of Zimbabwe, a country where an estimated 30% of the adult population are infected with HIV (13,15). This rise may be temporary however as it reflects current political instability of the country.

Table 1.5: Numbers of applications received for asylum in the UK, excluding dependents, by country in Africa

Nationality	2002(prov) (13)	% change 2001/2002	HIV Prev.(%) (15)
Zimbabwe	7,655	258%	30
Somalia	6,540	2%	1
Dem. Rep. Congo	2,215	62%	4
Angola	1,420	39%	2
Eritrea	1,180	90%	3
Sierra Leone	1,155	-41%	7
Nigeria	1,125	39%	4
Uganda	715	48%	5
Burundi	700	15%	5
Ethiopia	700	14%	12

Migrants are geographically much more concentrated than the GB population as a whole, with the majority living in London (16). Recently, increasing numbers of migrants have been dispersed throughout GB since the set up of the National Asylum Support Service (NASS), a service which provides accommodation and subsistence for asylum seekers in GB. Asylum seekers supported in NASS accommodation are dispersed throughout GB and the authorities with the highest populations of dispersed asylum seekers are: Glasgow, Birmingham, Leeds, Liverpool, Newcastle, Coventry, Manchester, Bradford, Sheffield and Nottingham (13).

1.3: HIV/AIDS amongst women: an overview

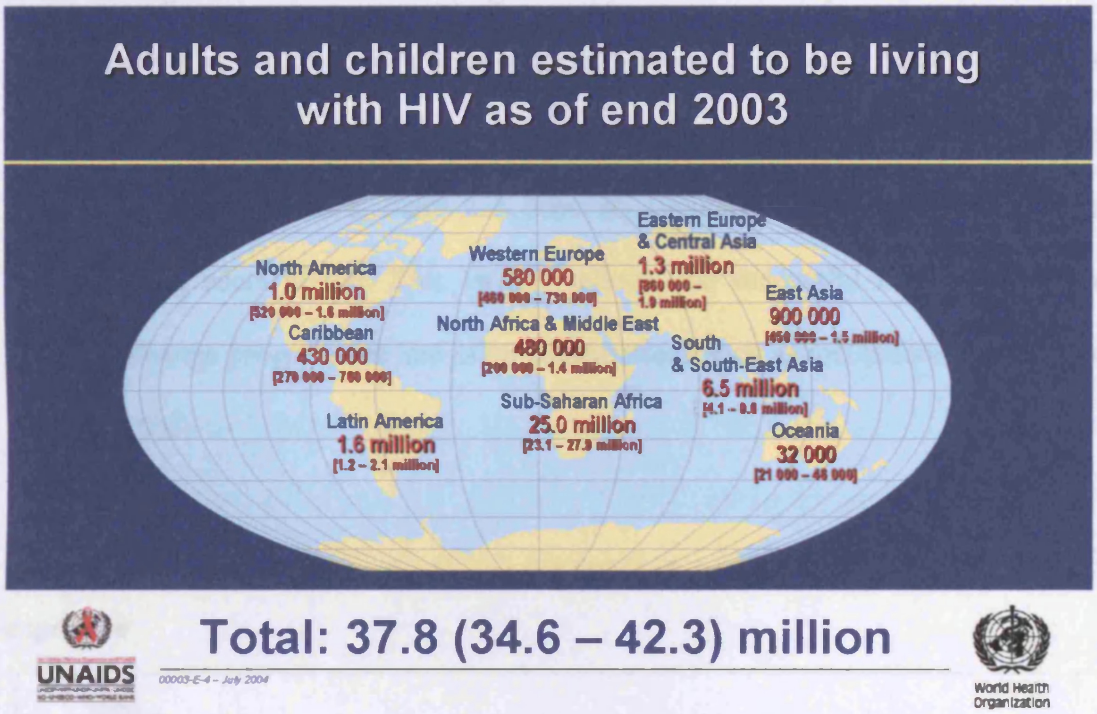
1.3.1: Introduction

Human Immunodeficiency Virus (HIV) and Acquired Immuno-Deficiency Syndrome (AIDS) remains a relatively new, incurable, clinically complex disease with a long incubation period between infection and detectable disease. Infection is associated with high morbidity and high treatment and care costs (17).

Globally, this disease carries a large health burden, with some countries feeling the weight of this burden more than others (Figure 1.3). Sub-Saharan Africa (SSA) remains the region worst affected by the HIV/AIDS epidemic, with an estimated 25 million people living with HIV in 2003 (1). The AIDS epidemic in Eastern Europe and Central Asia has shown no signs of diminishing and is being driven by widespread risky behaviour, including injecting drug use. Over 6 million people in South and South East Asia and nearly 1 million people in East Asia were living with HIV in 2003 and recently the epidemic has spread into areas where there was little or no HIV present, including China. In high-income countries such as GB the number of people living with HIV continues to rise, largely due to widespread access to antiretroviral treatment which has delayed disease progression (18). There is evidence that prevention activities in several high-income countries are not keeping pace with the changes occurring in the spread of HIV (1).

This section provides an overview of the epidemiology of HIV infection in GB and includes a description of the main transmission routes of infection and methods of surveillance, and then focuses on the epidemiology of HIV amongst women, the population group of interest for this thesis. As this project specifically focuses on the use of data from pregnant women, a description of HIV in pregnancy is provided.

Figure 1.3: Adults and children estimated to be living with HIV/AIDS at the end of 2003

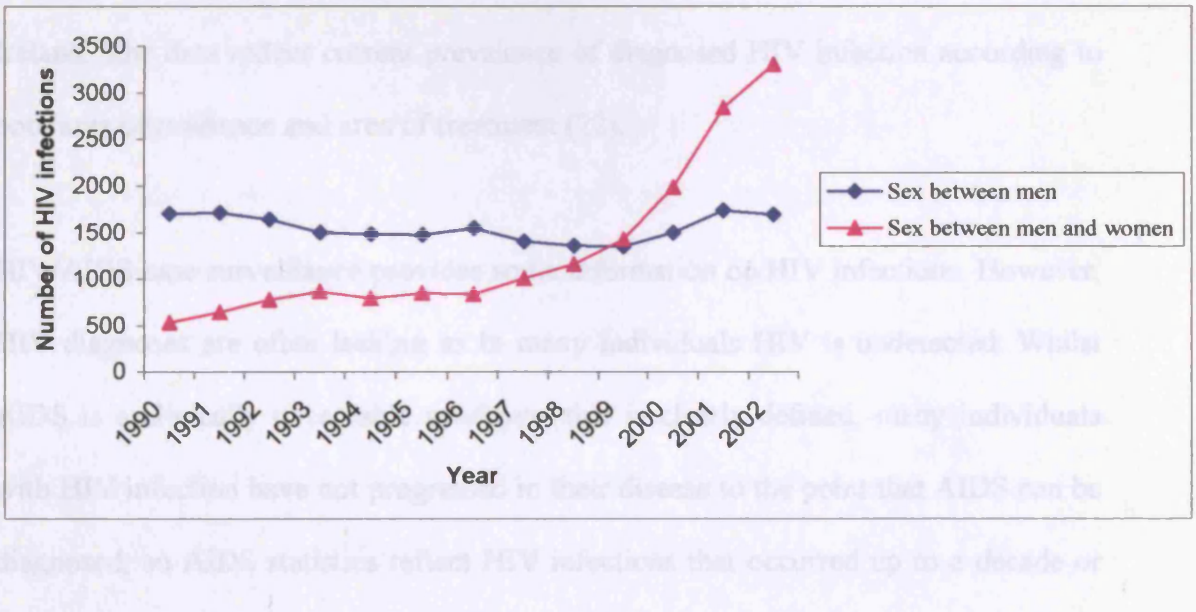


1.3.2: Transmission routes of infection in GB

An HIV/AIDS reporting system was first established in the UK in 1982 (17). Since then the number of HIV reports have increased annually and the total of 5,542 new diagnoses in 2002 was almost double the 2,814 diagnoses in 1998 (19). By contrast, the numbers of AIDS diagnoses and deaths in HIV-infected individuals has declined after the introduction of effective therapies (Highly active anti-retroviral therapy

(HAART)) in the mid-1990's (18). Men who have sex with men remain the group at greatest risk of acquiring HIV infection in GB. While homosexual transmission still accounts for the largest percentage of HIV infection, the proportion infected heterosexually increases yearly and this is mirrored by an increasing proportion of HIV infection due to vertical transmission. Since 1999, the number of new HIV diagnoses in heterosexuals has exceeded the number of new diagnoses in homosexual/bisexual men, reflecting a large and increasing impact of migration from areas of high HIV prevalence (Figure 1.4). Blood/blood products transfer and injecting drug use account for decreasing proportions of infection yearly (19). Apart from sudden outbreaks of HIV amongst injecting drug users (IDUs) in Edinburgh and Dundee in the mid-1980's, there has been no evidence of significant HIV spread amongst drug users in GB. This largely reflects the successful implementation of needle exchange programmes and other interventions such as methadone maintenance therapy (20).

Figure 1.4: Numbers of newly diagnosed HIV infections by probable route of exposure



1.3.3: Methods of surveillance in GB

As HIV has a long incubation period between infection and detectable disease, multiple sources of information are needed to fully understand the extent of the HIV epidemic. Surveillance systems in GB monitor both diagnoses of HIV infection through voluntary reports from clinicians and laboratories and levels of undiagnosed infection in the population through the Unlinked Anonymous (UA) programme. As the surveillance data are used in analyses throughout the thesis, more detailed methodology for the surveillance systems is provided in chapter 3.

New HIV and AIDS diagnoses are received from laboratories and clinicians and reported to the Health Protection Agency (HPA) Communicable Disease Surveillance Centre (CDSC) and the Scottish Centre of Infection and Environmental Health (SCIEH) to form a national HIV/AIDS surveillance system. The national data are made available as quarterly surveillance tables and other reports (19,21). As well as reports of new diagnoses of HIV/AIDS, numbers of persons currently receiving HIV-related care are collated as part of the National Survey of Prevalent HIV Infections Diagnosed (SOPHID), which was set up in 1997 in England, Wales and Northern Ireland. The data reflect current prevalence of diagnosed HIV infection according to both area of residence and area of treatment (22).

HIV/AIDS case surveillance provides some information on HIV infections. However, HIV diagnoses are often lacking as in many individuals HIV is undetected. Whilst AIDS is a clinically observable syndrome that is clearly defined, many individuals with HIV infection have not progressed in their disease to the point that AIDS can be diagnosed, so AIDS statistics reflect HIV infections that occurred up to a decade or more in the past (17). For these reasons, monitoring HIV seroprevalence is a more accurate way of assessing the extent of the epidemic. Arguably the best method for such monitoring is UA testing of residues of blood samples taken for other clinical purposes, since in theory this should lessen both participation and selection bias (2). An accessible population is selected and the residual of blood samples collected for other clinical purposes are tested for HIV after the irreversible elimination (unlinking) of all personal identifying information from each specimen. The populations that are currently part of the UA programme in GB are genito-urinary medicine clinic attenders, injecting drug users, antenatal clinic attenders, newborns (dried blood spot testing) and pregnant women seeking terminations (23).

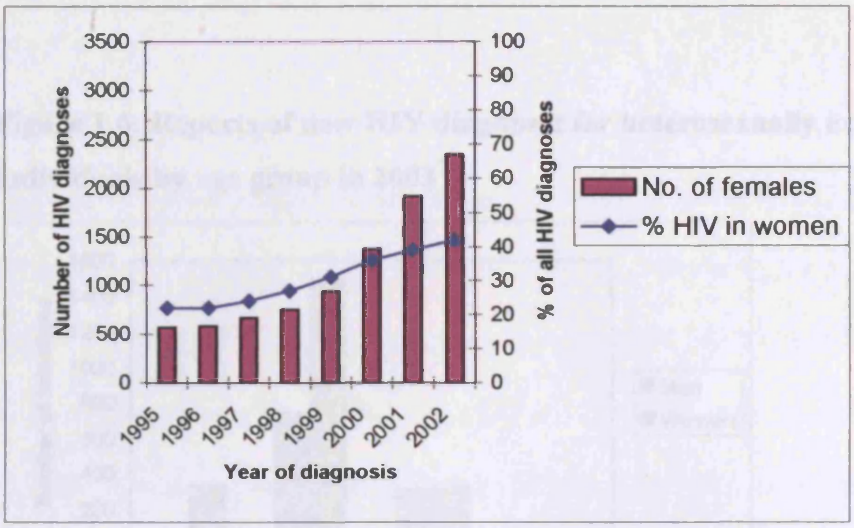
In addition to the surveillance systems at CDSC and SCIEH, researchers at the Institute of Child Health (ICH) monitor numbers of reported HIV-infected pregnant women, diagnosed either before, during or after pregnancy, and numbers of children born to HIV infected mothers through the National Study of HIV in Pregnancy and Childhood (NSHPC). Children are followed up until infection status outcome is established (24-25).

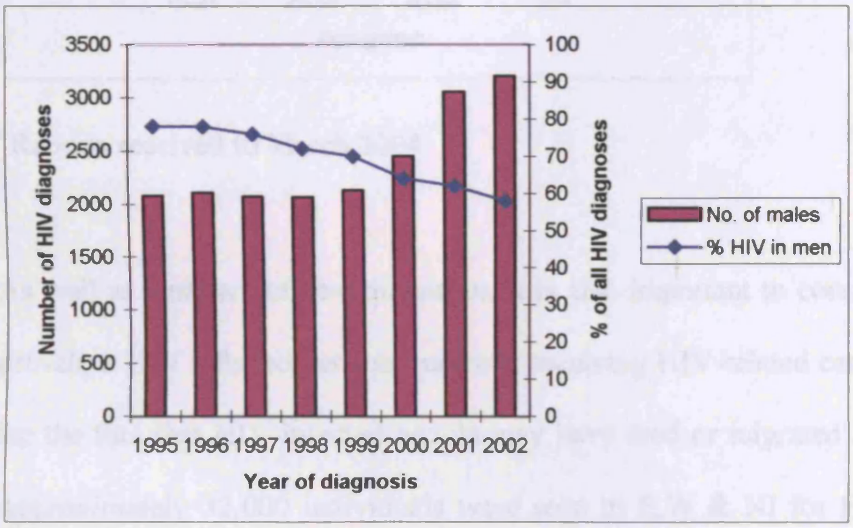
1.3.4: Characteristics of HIV/AIDS diagnoses amongst women in GB

In 2002, women accounted for 42% of new HIV diagnoses, and the proportion of all cases that are female continues to grow (Figure 1.5) (19). Most of the new HIV diagnoses in females (including women and children) were attributed to heterosexual contact (96%), with few cases being attributed to injecting drug use (1%), mother to child transmission (MTCT) (2.5%) and blood/blood products transfer (0.5%). The majority of heterosexually acquired cases were recorded as having probably been acquired in Africa, predominantly East Africa (for example Uganda). The impact of the HIV epidemic in South East Africa in GB is however growing and in 2002 Zimbabwe was the predominant probable country of infection (26). Where year of arrival in the UK was available (839/1757), the majority (60%) of women who had probably been infected abroad had arrived in this country in the previous 3 years (unpublished data, CDSC reports).

The number of women who were reported as having acquired HIV heterosexually from a "high risk" partner (a bisexual man, IDU or someone infected through blood transfusion or blood factor treatment) was small; in 2002 only 2% of heterosexually acquired infections were in this category and most of these 'high risk' partner infections occurred in the UK. In contrast, women who acquired HIV heterosexually in the UK from a partner who themselves acquired their infection heterosexually, formed 10% of the new diagnoses in 2002. This is a decrease from 16% in 1995.

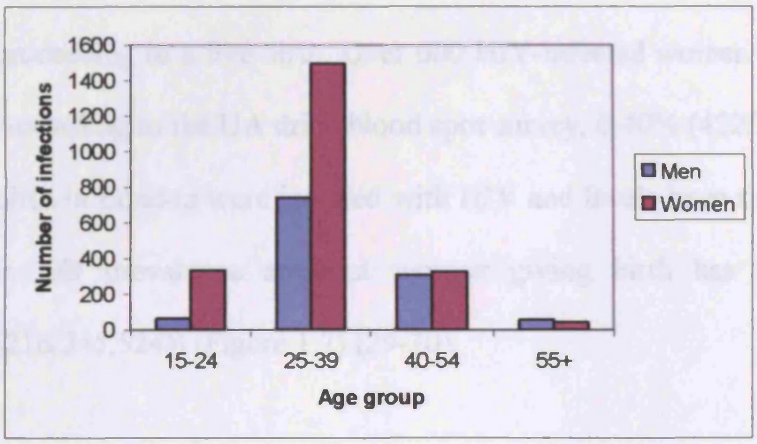
Figure 1.5: Number of HIV diagnoses amongst adults and % of reports in GB: Data reported to June 2003





Most reports of HIV diagnoses were amongst women of childbearing age. Generally women were younger than men at HIV diagnosis and this difference was particularly evident for heterosexually-acquired infections (Figure 1.6) (19). Of the 1,993 women infected through heterosexual exposure in 2002, 16% were aged 15-24, 68% aged 25-39, 14% aged 40-54 and 2% aged 55 and above. Eighty four percent of infections among 15-24 year olds reported in 2002 were among females. Studies in Africa have examined factors which may be responsible for this disparity and have concluded that either women are more susceptible to infection (27) or that young women are becoming infected by older sexual partners (28).

Figure 1.6: Reports of new HIV diagnoses for heterosexually exposed individuals by age group in 2003[1]



[1] Reports received to March 2004

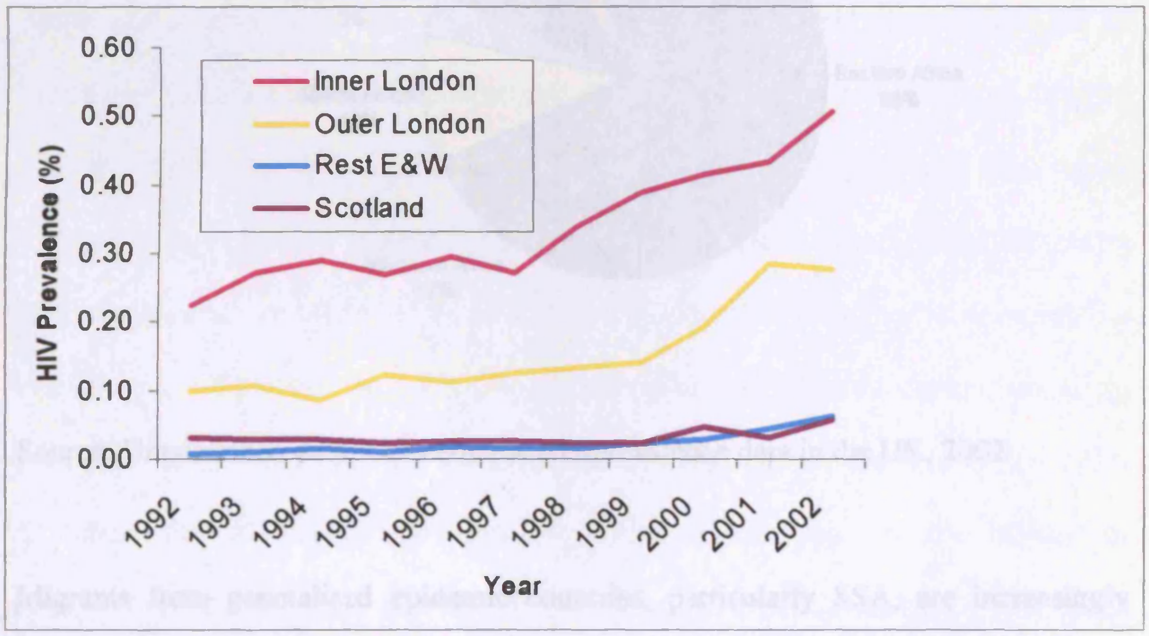
As well as numbers of new diagnoses, it is also important to consider the number of prevalent HIV infected persons currently receiving HIV-related care. This data allows for the fact that HIV infected people may have died or migrated out of the country. Approximately 32,000 individuals were seen in E,W & NI for HIV-related care in 2002. Of these, 28% (8,967) were women, representing a 3-fold increase in the number of women being seen for treatment and care since 1997 (Unpublished data, SOPHID survey 2002).

Whilst the vast majority of those HIV-infected are younger adults, the improvements in HAART have meant that increasing numbers of HIV-positive women are reaching older age. Data from SOPHID indicated that the number of women aged >=45 years accessing HIV-related services more than doubled between 1997 and 2002 (unpublished data, SOPHID data 2002).

1.3.5: Seroprevalence of HIV infection amongst neonates

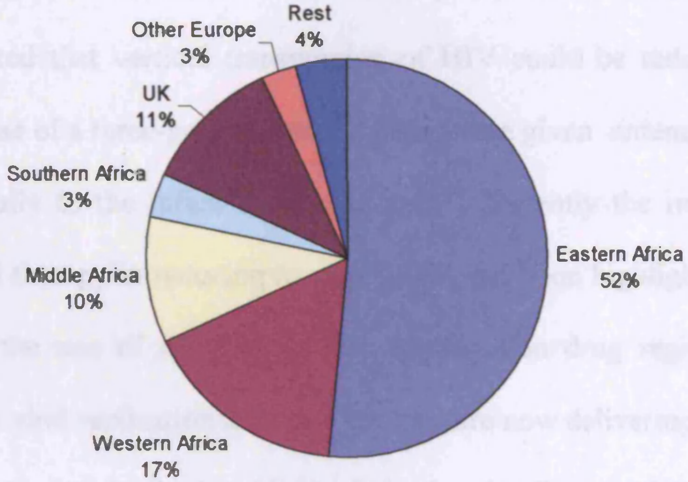
HIV prevalence amongst neonates reflects levels of HIV infection amongst women proceeding to a live birth. Over 600 HIV-infected women gave birth in GB in 2002. According to the UA dried blood spot survey, 0.40% (422/105,817) of women giving birth in London were infected with HIV and levels have risen since 1997. Elsewhere in GB prevalence amongst women giving birth has remained lower (0.063% (216/345,524)) (Figure 1.7) (29-30).

Figure 1.7: Trends in HIV infection in pregnant women giving birth as assessed by neonatal seroprevalence in GB



Important demographic variations in HIV prevalence amongst women giving birth were apparent. Analyses showed that a much greater proportion of HIV infected pregnant women born in SSA were HIV-positive compared with those born in the UK (Figure 1.8); Of all HIV-infected women giving birth in 2001-2002 for whom country of birth was known (571/651), 82% (464 of 571) were born in SSA. Women born in Zimbabwe (10.2%), Zambia (8.4%) and Uganda (8.3%) (all countries classified as Eastern or South Eastern Africa) had the highest HIV prevalence.

Figure 1.8: Percentage distribution of HIV seropositive samples amongst pregnant women according to country of birth: 2001-2002



Source: Unpublished data, UA neonatal seroprevalence data in the UK, 2002

Migrants from generalised epidemic countries, particularly SSA, are increasingly driving the HIV epidemic not only in the UK but throughout Western Europe. Two thirds of all heterosexually acquired HIV infections diagnosed during 1997-2002 in Western Europe were in people from countries with generalised HIV epidemics, reflecting the worsening of the HIV epidemic in Africa and changing worldwide migration patterns (31). The effect of the African epidemic on national HIV situations differs between European countries and reflects past colonial history and current migration patterns. The implications have been substantial within GB due to the links with Eastern and Southern Africa, countries which have a particular high HIV prevalence (1).

1.3.6: HIV screening during pregnancy

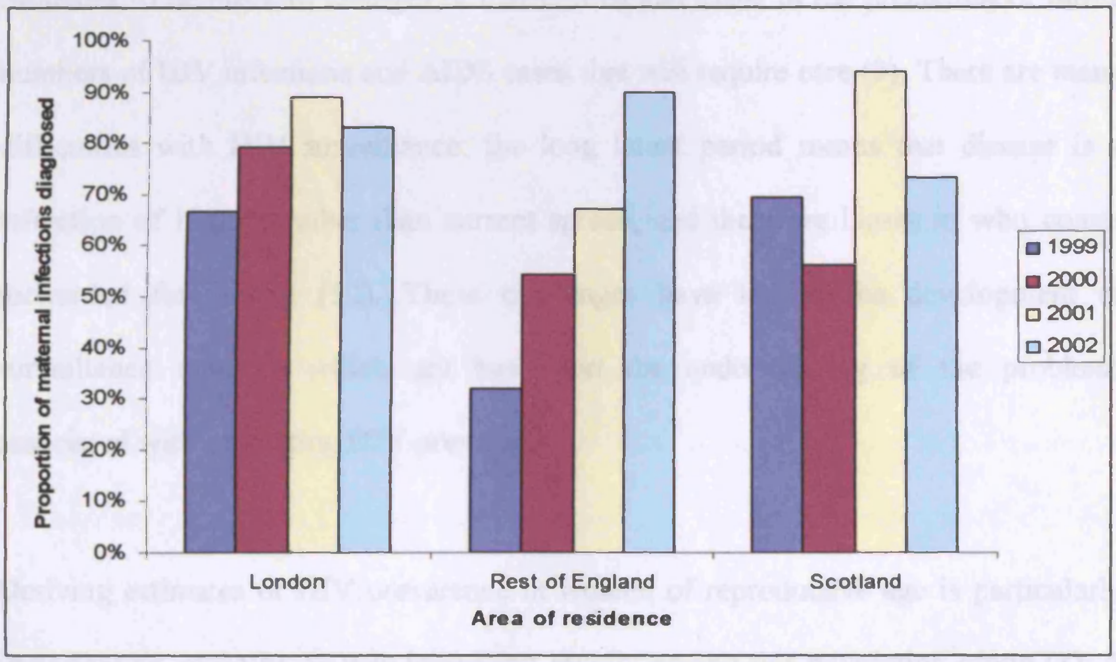
In Europe, in the absence of any interventions, HIV infection in pregnancy is associated with a risk of mother to child transmission (MTCT) of between 15-20% with the higher levels in mothers who breastfeed (32). The ACTG076 trial published in 1994 demonstrated that vertical transmission of HIV could be reduced by two thirds through the use of a three-part regimen of zidovudine given antenatally, during labour and postnatally to the infant for 6 weeks (33). Recently the importance of potent antiretroviral therapy in reducing levels of RNA has been highlighted (34-36). This has initiated the use of more aggressive combination drug regimens which maximally suppress viral replication and many women are now delivering babies with undetectable maternal viral loads. In addition, Nduati and colleagues have reported a significantly higher rate of MTCT in infants who are breastfed rather than given formula feed (37) and trials have shown elective caesarean section (CS) before onset of labour and rupture of membranes significantly reduces the risk of vertical transmission compared to both vaginal and emergency CS deliveries (38-39). With antiretrovial therapy, delivery by CS and avoidance of breastfeeding, transmission was shown to be reduced to well under 2% (34-36). There are also increasing benefits for the woman herself knowing that she is infected, as early diagnosis of HIV infection allows the mother to be prescribed HAART for her own health. The British HIV Association (BHIVA) published guidelines for prescribing antiretroviral therapy in pregnancy advocating the use of these drugs as the best prospect for prolonged health in pregnant women as well as reducing vertical transmission (40) (www.bhiva.org/guidelines/2003/hiv/index.html accessed July 2004).

In response to results from trial ACTG076, an appreciation that HIV infection was transmitted through breastfeeding and the knowledge that within GB, as elsewhere, the majority of HIV infection in children was attributed to MTCT (41), the UK Departments of Health recommended that all women resident in areas of high prevalence, for example London, and women considered to be at high risk of infection should be offered antenatal HIV testing. These recommendations were made in 1992 and again in 1994 (42-43). Following this in 1996 a set of guidelines for pre-test discussion on HIV testing were produced simplifying previous practice which tended to emphasise lengthy pre-test counselling (44-45). Despite these recommendations, most maternal infections remained undiagnosed and high numbers of children were still presenting with an AIDS-defining illness as the first indication of the mothers HIV infection (6). This finding led in 1998 to a professional initiative by an intercollegiate working party group, the aim of which was to increase the uptake of antenatal testing and consequently the reduction in paediatric AIDS cases (46). The Working Party made a series of 20 recommendations on improving antenatal HIV testing, the focus of which were to integrate antenatal HIV testing with testing for other infections. More recently (1999) the Government announced a major policy development and the establishment of national targets for antenatal HIV testing in England (47). Targets were set to increase both the uptake of antenatal HIV testing to

90% and the proportion of HIV infections diagnosed prior to delivery to 80% by the end of 2002. Guidance was also issued for the health service in Scotland and Wales on universal antenatal HIV testing (48-49).

The proportion of maternal infections diagnosed before and during antenatal care can be estimated by comparing reports of diagnosed HIV-infected pregnant women, which is collected through the National Study of HIV in Pregnancy and Childhood (described further in chapter 3), with the number of seropositive pregnant women estimated from the UA surveys. Since the 1998 professional initiative, there has been a steady increase in the proportion of HIV-infected women diagnosed before delivery and in 2002 this was over 80% (Figure 1.9).

Figure 1.9: Estimated proportion of HIV infected pregnant women diagnosed before delivery*



* These estimates are subject to reporting delay and data for 2002 in particular is likely to rise as more diagnosed infections in pregnancy are reported

Source: Unlinked Anonymous Seroprevalence Monitoring Programme (50)

The improvement in timely diagnosis in women has resulted in a substantial decrease in the number of infected infants (51). The drastic reduction seen in perinatal transmission and the availability of HAART may have changed pregnancy decision making amongst HIV-infected women and this is discussed in more detail in chapter 2. Such a change in reproductive behaviour would have been reflected in changes in estimated levels of HIV amongst pregnant women in seroprevalence studies as HIV-positive women would have an increased likelihood of having a live birth and therefore appearing in neonatal seroprevalence surveys.

1.4: Importance of monitoring HIV prevalence amongst women

Accurate HIV prevalence estimates have important public health uses as they give an appreciation of the total burden of infection within the population, allow objective estimates to be made of changes in that burden and assist in the prediction of future numbers of HIV infections and AIDS cases that will require care (2). There are many difficulties with HIV surveillance: the long latent period means that disease is a reflection of historic rather than current spread; and there are biases in who comes forwarded for testing (52). These challenges have led to the development of surveillance methods which are based on the understanding of the problems associated with estimating HIV prevalence.

Deriving estimates of HIV prevalence in women of reproductive age is particularly important as, globally, HIV is increasing rapidly among this population group (1). A population frequently chosen for this purpose is antenatal clinic (ANC) attendees. Pregnant women are a stable sub-group of the total heterosexually active population and the trend in HIV infection in pregnant women should mirror that in the heterosexual population. The WHO stated in their guidelines in 1989 that UA surveys are generally considered an accurate and effective method for public health surveillance (53). In a 1998 document of the WHO and The Joint United Nations Programme on HIV/AIDS (UNAIDS), it is stated that UA Surveillance through ANCs remains the best available option for HIV surveillance (54). An alternative method of monitoring HIV seroprevalence amongst pregnant women is to test residual neonatal blood spots for passively acquired maternal antibodies, an approach used in GB (55). Results from this survey, which have already been summarised in this chapter, are analysed further throughout this thesis.

1.5: Developments of methods for estimating HIV prevalence

Neonatal seroprevalence data have already been used to provide estimates of HIV infected people in Britain using direct and indirect methods.

In the direct method, estimates of the total number of HIV infections in the population were calculated through combining data from three unlinked anonymous surveys with estimates of the size of the population in various exposure categories derived from the National Survey of Sexual Attitudes and Lifestyles, census 2001 population estimates and reports of diagnosed prevalent HIV infections. The total population of GB was divided into mutually exclusive behavioural categories relevant to HIV infection risk (homosexual men, IDUs and low risk heterosexuals as represented by pregnant women). The undiagnosed HIV prevalence for each group was multiplied by its population size to determine the total number of undiagnosed HIV infections. These were then added to the prevalent diagnosed HIV infections within each group (4-5). This technique is currently the preferred method for providing HIV estimates for the UK (30) and in 2002 it was thus estimated that 49,500 adults aged 16 years and over were living with HIV. Approximately a third of the total numbers of HIV infections were estimated as being undiagnosed (Table 1.6).

Indirect methods are based on the proportion of persons recently diagnosed with AIDS whose first positive HIV test was probably before any illness associated with their AIDS diagnosis (56). This proportion is assumed to indicate the proportion of all persons currently infected with HIV without AIDS who have had a voluntary HIV test. One key assumption in this method is that the incubation period in persons with diagnosed HIV infection is the same as in undiagnosed HIV infected individuals. Since 1997 this method has been severly compromised by the effects of anti-retroviral therapies as fewer diagnosed HIV infected individuals now progress to AIDS.

Table 1.6: Estimated prevalent HIV infections, diagnosed and undiagnosed among adults[1] in the UK at the end of 2002

Route of probable infection	Number diagnosed[2]	Number undiagnosed [3,4]	Total
Homo/bisexual men	17,100	5,500 (24%)	22,600
Injecting drug use	1,400	300 (18%)	1,700
Sex between men and women	15,100	9,400 (38%)	24,500
Blood products [5]	700	0	700
Total	**34,300**	**15,200 (31%)**	**49,500**

1 Aged 15-59 inclusive, excludes those who have died during the year
2 Numbers diagnosed obtained from SOPHID and SCIEH, adjusted for under-reporting and failure to access services
3 Numbers undiagnosed derived for England and Wales using data from SOPHID, NATSAL and the UA programme in an extension of a method previously described (4)
4 Numbers undiagnosed for Scotland estimated by using exposure group specific scaling factors derived for England and Wales
5 All cases infected by blood and blood products or tissue were assumed to be diagnosed

Finally, back-calculation, a different type of technique which has not relied on the use of seroprevalence data, has been used to provide estimates of HIV incidence based on knowledge of the incubation period from HIV infection to AIDS and of AIDS incidence over time (57). From this estimated HIV incidence, after adjusting for annual mortality and inward and outward migration, estimates of overall HIV prevalence (both diagnosed and undiagnosed) could be derived. Again, however, advances in AIDS treatment have made this technique inappropriate and adjustments for migration patterns in and out of the country have been inadequate.

Other methods have also been developed for the production of HIV estimates. The number of HIV-infected persons in the US was estimated by simply applying observed prevalence rates amongst pregnant women proceeding to delivery to all women derived from census data, stratifying by race, age and region of residence (58). A UNAIDS/WHO Working Group on Global HIV/AIDS and STD surveillance produced country-specific estimates for HIV infection. For developing countries with generalized epidemics, prevalence estimates were based primarily on surveillance data collected from women attending antenatal clinics. The prevalence estimate for women was then used to estimate the prevalence among men, based on the assumed female-to-male ratio (59).

1.6: Factors to consider when extrapolating neonatal prevalence data to the general female population

Concern has been raised over the representativeness of sentinel surveillance using pregnant women. The extrapolation of neonatal seroprevalence data to the general population assumes that HIV-infected women have an equal probability of becoming, and staying, pregnant as uninfected women and that there is no differential fertility between persons at high and low risk of HIV infection (7,60); in other words fertility is assumed to be independent of HIV risk. There are a number of reasons why this is unlikely to be the case, especially in countries such as GB where underlying fertility is relatively low and HIV infection is high in sub-groups with high fertility (7). There are important social and behavioural differences between pregnant and non-pregnant women, which can make the prevalence of HIV in pregnant women different from that in all women. A substantial body of literature which has reviewed fertility in HIV- positive women exists and is presented in chapter 2.

In order to determine whether HIV seroprevalence in the sentinel group truly represents that of the population at risk, it is necessary to assess the relative likelihood of an HIV-infected individual being included in the sentinel group compared to any other member of the population. The mathematical relationship is sometimes referred to as the relative inclusion ratio or risk (RIR), with an RIR above unity if an HIV-infected individual is more likely to be included in the sentinel group than an uninfected individual (60). RIRs could also change over time producing spurious trends in sentinel group prevalence despite an unchanging prevalence and effectively preventing estimating HIV incidence from seroprevalence data (61).

RIRs which differ significantly from unity may reflect behavioural, socio-economic and/or cultural differences between infected and uninfected individuals (60). There may be different influences on the RIR:

Pre-diagnosis influence: The RIR may differ from unity because of behavioural or demographic risk prior to diagnosis of HIV infection. Differential coverage of neonatal dried blood spot screening by ethnicity has been documented (62). In particular, coverage was poorer for infants in the African ethnic group compared to White infants (63). Since HIV prevalence is higher in African women in GB, extreme under-coverage of African infants in the dried blood spot survey could in theory result in substantial underestimates of HIV prevalence. In practice however there is evidence that this is not the case in GB (62,64).

Post-diagnosis influence: The RIR may differ from unity because of behavioural or clinical consequences following diagnosis of HIV infection. For example, some studies have shown that higher proportions of women who are seropositive for HIV infection elect for a termination of pregnancy compared to seronegative women, although sample sizes in these studies were small and the differences did not reach statistical significance (65-67). However, if such a differential exists, the serosurvey of HIV infections in women having a termination of pregnancy are likely to produce higher estimates of seroprevalence of HIV infection in heterosexual women than the survey of antenatal clinic attenders or the neonatal dried blood spot survey.

Natural history influence: The RIR may fall below unity as a consequence of disease progression. As a woman becomes unwell she may be less likely to become pregnant.

Interpreting HIV prevalence data from pregnant women is therefore difficult and estimates are likely to be biased if factors associated with both fertility and HIV risk are not accounted for. For the purposes of this thesis, the assumptions associated with extrapolating neonatal prevalence to the general population were reviewed and summarised below:

Assumption 1: Groups in the population at high and low risk of HIV infection have similar underlying fertility patterns.

In GB women born in SSA and IDUs have the higher HIV prevalence (30). Whilst data relating to fertility in IDUs are lacking, African women are known to have higher fertility rates than the White population in GB (8). Assumption 1 is therefore violated and HIV prevalence in the general population may be overestimated to an unknown extent if differential fertility patterns of populations at high or low risk of HIV are not taken into consideration. In addition the size of population sub-groups with differing HIV risk and fertility patterns in GB may change due to migration or other factors, again complicating our understanding of trend data amongst pregnant women.

Assumption 2: Knowledge of HIV status does not alter reproductive decisions

HIV-infected women may reduce their number of live births after HIV diagnosis. Results from studies comparing live birth rates before and after HIV diagnosis in cohorts of HIV-infected women found that live births decreased after HIV diagnosis (68). Whilst a fall in birth rates could be explained by factors other than knowledge of HIV status, this assumption needs further investigation. Since these studies were carried out, treatments to delay HIV disease progression in adults and interventions to reduce MTCT of HIV have improved substantially over the last few years (33-35,37-38,69) and routine antenatal HIV screening programmes have recently been widely implemented in GB (50). It is possible that these developments may influence intentional fertility decisions amongst HIV-infected women.

Assumption 3: HIV-infected women have the same biological ability to become pregnant and carry a pregnancy to term as HIV-uninfected women.

It is generally assumed that HIV status does not influence unintentional fertility except in advanced disease (discussed further in chapter 2). However evidence to confirm or refute this assumption is limited and further research is needed. It is unclear to what extent a violation of this assumption would operate in GB and bias the use of neonatal seroprevalence for the general population.

1.7: Methods to adjust neonatal seroprevalence data

Limited attempts have already been made to devise methods to adjust neonatal seroprevalence data to reflect general population prevalence. Zaba et al suggested a method for adjustment for the developing world in which the HIV prevalence is determined separately for ANC attenders with and without children (70). A separate correction factor was applied to each group, based on the HIV prevalence ratio for ANC attenders versus women in the general population among parous and nulliparous women. This method was shown to work well in two African populations with low contraceptive use. This method was then validated in different populations by Changalucha et al and Fabiani et all, showing that in some centres more accurate estimates were obtained (71-72). This correction factor is most useful in developing countries where contraceptive use is low and fertility is high and where women acquire HIV at a young age.

Recently a method for adjusting HIV seroprevalence in pregnant women was devised in the UK using estimates of fertility rates before and after HIV diagnosis by risk group (68) and applying these rates to neonatal seroprevalence data (73). Birth and termination rates from women known to be HIV infected were derived from the MRC collaborative Study of Women with HIV. These rates were then compared with those for HIV-uninfected women using vital statistics to generate a fertility ratio. This ratio was then applied to neonatal seroprevalence data to estimate population prevalence among all women. Whilst this method was simple and demonstrated that fertility effects were important when applied to neonatal seroprevalence results, the data available on live births amongst HIV-infected and uninfected women was limited. In order to improve these estimates of HIV infection in the general population it is therefore important to understand the numerical relationship between HIV and fertility fully to then use this information to develop a robust adjustment model.

The purpose of this thesis was therefore to estimate the HIV prevalence in the adult female population in GB using neonatal data. The biases associated with each assumption discussed above were assessed and quantified and used to extrapolate neonatal data to the general female population.

1.8: Key Points

1. HIV estimates for the general female population are currently based on unadjusted neonatal seroprevalence data. It is recognised that these estimates are likely to be biased as factors associated with differential fertility between persons at high and low risk of HIV have not been accounted for.

2. Previous research has suggested HIV-infected women may experience a reduction in the number of live births after diagnosis. It is not known whether this decline could be explained by knowledge of HIV status or other factors. It is also unknown whether this remains after allowance has been made for the total number of births these women would have wanted to have in the absence of HIV.

3. An increase in neonatal HIV seroprevalence has been recorded in all parts of GB since 1997, particularly London. It is unclear whether this rise corresponds to a rise in HIV in the general female population, or whether fertility decisions amongst HIV-infected women have changed due to increasing availability of treatments and interventions. Alternatively the size of groups at risk of HIV in GB may have changed.

4. Universal antenatal HIV screening has been implemented in GB and increasing proportions of previously unidentified HIV-infected women are having their infection diagnosed. The impact of improved antenatal testing, and possible earlier diagnosis, on pregnancy outcome is not known.

1.9: Outline of thesis

Chapter 2 consists of a review of the literature on fertility in HIV-infected women and explores further the biases associated with extrapolating unadjusted neonatal seroprevalence data to the general female population. Chapter 3 describes the type of analyses done and the datasets used and provides a framework of how the neonatal and other data sources will be used for the purposes of this project. The extent of bias associated with the assumption that groups in the population at high and low risk of HIV infection have similar underlying fertility patterns, is analysed and presented in chapter 4. Chapter 5 presents estimates of fertility amongst HIV-infected women using established British and European datasets. The methodology and analyses of a cross-sectional questionnaire study, the main survey of the PhD project, is then presented (chapter 6). Chapter 7 uses all analyses from chapters 4-6 to develop a model for estimating female prevalence in the general population from that in pregnant women. Finally, chapter 8 consists of the discussion and recommendations for future work.

Chapter 2: Association of HIV and fertility

2.1: Introduction

During the past decade, there has been a dramatic increase in the number of women infected with HIV. One of the most prominent features of HIV infection is that it is usually diagnosed during the peak reproductive years. For this reason, there has been long standing concern regarding the obstetric implications of HIV infection.

Decisions around childbearing are complex and many factors including maternal HIV infection status may influence these decisions (Table 2.1). With the improvement of anti-retroviral therapy and as more interventions to reduce the risk of vertical transmission are identified, infected women's reproductive decisions may have been influenced.

Table 2.1 Decisions around childbearing

Many factors may influence an HIV-infected women's decision to have a child or continue with a pregnancy. Adapted from Newell et al 1997 (74)
General
Sociocultural factors
Existing family size
Past reproductive history
Attitudes towards and policies for termination of pregnancy
HIV-related
Maternal health status
Knowledge of risk of vertical transmission
Availability of interventions to reduce risk of vertical transmission
Family support
Availability of treatment to delay disease progression

This chapter reviews the literature on the association of HIV and fertility. It begins with a review of the magnitude of the differences between the fertility rates of HIV-infected and uninfected women. This has been established by gathering evidence from prospective studies of the fertility of HIV-positive and HIV-negative women. Secondly, the comparison of estimates of the prevalence of HIV among pregnant women to all women of reproductive age is investigated. Finally, other studies that look at the association between HIV and fertility are reviewed, the majority of which look retrospectively at birth histories and pregnancy outcomes for women of known HIV status. Whilst many studies reviewed in this chapter were carried out in Africa, findings were considered relevant to this thesis as the majority of HIV infection among women in GB is associated with time spent in sub-Saharan Africa (SSA) (30).

2.2: Prospective studies of fertility rates among HIV-positive and negative women.

Several prospective studies have been carried out to determine the fertility rates among women with and without HIV (75-78). These studies have all been located in SSA where the epidemic is older and more severe than GB. The main results of these studies are shown in Table 2.2. In all four studies, a lower fertility ratio was found among HIV-infected women relative to the HIV-uninfected women and odds ratios ranged from 0.73-0.81.

Women recruited into the studies were either from a hospital following the birth of a child (75) or from a community setting (76-78). Since both the HIV-infected and uninfected women recruited from the hospital setting were of proven fertility, their subsequent reproductive performance is likely to be higher than that of women in the population as a whole. Women suffering from primary and secondary sterility would not have appeared in this sample nor would women who were not in active sexual partnerships. In addition, a relatively high number of hospital attenders were lost to follow-up during the first year, and the infant mortality rate in the children of these women was much higher than women who remained in the study. It is difficult to predict what the fertility rates would have been in the infected women lost to follow-up.

Whilst the four studies reviewed showed a reduction in pregnancy rates in HIV-infected women compared to HIV-uninfected women, it remains unclear whether this effect was due to biological, behavioural or social factors. Fertility rates may have declined in HIV-positive women following knowledge of infection and subsequent use of contraceptives that would both prevent pregnancy and HIV transmission. However, in 2 studies the majority of women were unaware of their status and use of contraception in Africa is rare (76-77). Gray found reduced fertility in HIV-infected Ugandan women irrespective of knowledge of serostatus (77). Whilst in the Kinshasha study all women were aware of their status, few informed their sexual partner which in turn prevented consistent use of barrier contraceptives. The fertility rates in these women may have declined because of the intensive education and counselling which these women received in the programme. The women were made aware of their HIV infection status and the risk that this infection posed to future children and the importance of using condoms was repeatedly emphasised (75).

Previous research has shown women with histories of Sexually Transmitted Infections (STIs) have lower fertility rates than similarly aged women without a history of an STI (79). Gray found higher proportions of HIV-positive women had been infected with syphilis in the past, exposing them to higher risks of foetal loss. When cross-infection with syphilis was accounted for, there was still a significant reduction in fertility in HIV-positive women (77). Ross investigated gravidity (likelihood of being pregnant) as well as fertility (likelihood of having live births) and found that almost a half of the association between HIV infection and pregnancy incidence was contributed by low gravidity prior to HIV infection rather than a direct effect of the HIV disease itself. The authors concluded that STIs and HIV are intricately linked, and prior STI infection may increase susceptibility to both fertility problems and HIV infection (78).

HIV positive women who were symptomatic with HIV infection had lower fertility rates than asymptomatic HIV-positive women (75,77). It was not determined whether these lower rates were due to lower rates of sexual activity in HIV-positive women or due to a primary effect of HIV infection on fecundity (ability to have children). A study in 15 hospitals in Uganda of signs and symptoms associated with HIV found that amenorrhoea was a common symptom for AIDS in an African population (80). This was probably due to the severe weight loss that occurs in the later stages of HIV illness and is likely to be less common in developed countries where HIV-related treatments are widely available. There may also be repercussions for women's fertility from the biological effects of HIV on their infected partners, who may be further along in the course of disease progression and suffer from symptoms such as decreased production of spermatozoa (81). However, lower pregnancy rates were still observed in asymptomatic HIV-positive women than HIV-positive women with symptoms, so clinical AIDS cannot explain all the decrease observed.

In summary, little information was gathered on biological or social factors which would help to explain the discrepancy in fertility rates between HIV-positive and HIV-negative women. Few of the studies determined marital status of the women, health status of the partner or frequency of sexual activity and two of the studies did not include the presence of other STIs for inclusion in the analysis. Without such information, it is difficult to conclude anything more than an association between HIV and fertility.

Table 2.2: Prospective studies of fertility rates among HIV-positive and negative women: Developing countries

Author, year	**Ryder, 1991**	**Carpenter, 1997**	**Gray, 1998**	**Ross, 1999**
Location	Kinshasa, Zaire [a]	Masaka, Uganda [b]	Rakai, Uganda [c]	Masaka, Uganda [d]
Fertility Rate HIV positive (per 1000)	190.1	194.8	235	206
Fertility Rate HIV negative (per 1000)	265.4	212.3	301	254
Total no. HIV positive in study	238	332	692	80
Total no. HIV negative in study	315	3352	2382	96
Date	1986-90	1989-96	1994-6	1990-1997
Fertility Ratio (infected:uninfected)	**0.77** [e]	**0.74** [f] **(0.63-0.87)**	**0.73** [g]	**0.81** [h]

[a] Women recruited from hospital following birth of child. Number of pregnancies per 1000 women (annual)
[b] All women 15-49 residing in 15 neighbouring villages.
[c] All women 15-49 living in 56 communities.
[d] HIV infected women recruited in a HIV Natural History Cohort study
[e] adjusted for birth control
[f] adjusted for age
[g] adjusted for age, birth control and breastfeeding
[h] adjusted for age, lactation, sexual activity, illness and STI symptoms

2.3: Comparison of HIV prevalence estimates between pregnant women and women in the general population

A number of studies have assessed how well sentinel groups, in particular pregnant women, reflect prevalence in the general population (72,82-87). These studies have all been carried out in various countries within Africa, and involve comparing estimates amongst antenatal clinic attenders (ANC) with estimates from population-based surveys of women. In all studies, HIV prevalence among ANC was lower than the prevalence amongst women in the general population (Table 2.3). The ratio of HIV prevalence in pregnant women to HIV prevalence in all women ranged from 0.66 to 0.94.

A further study by Fontanet et al estimated the age and sex-specific HIV prevalence in the urban community setting of Addis Ababa, Ethiopia in 1994 (88). HIV prevalence among women was 6.9% and there was considerable variation in different areas of the city (0-21.3%). This data was compared with data collected from four antenatal clinics in Addis Abaha in 1996 and a substantially higher HIV prevalence rate was found in the pregnant women (17.8%). The authors suggested that this discrepancy to previous studies was because some women in the community, with behaviours at high risk of HIV, were reluctant to provide blood samples. Alternatively, an explanation for the prevalence difference could have been the 2-year interval between data collection from the general population and ANC surveys during a period when the epidemic may have been growing. In three other studies presented in Table 2.3 (Lusaka and Mposhi, Zambia and Kagera, Tanzania) the ANC sentinel survey and the general population survey were also carried out during different periods of time and this may complicate interpretation of results.

Whilst overall HIV prevalence was higher amongst women in the general population, in the youngest age group (15-19 years) prevalence was higher in antenatal women in some of the studies reviewed (72,82,84,86-87). This may be explained by the fact that women who begin sexual activity at an early age are exposed to the risk of both pregnancy and HIV. In the older age groups HIV prevalence represents the cumulative total of infection over a longer period of time. These women are more likely to be sexually inactive, due to the effects of sickness, separation and widowhood, and their fecundity will be increasingly affected by biological factors that increase in importance with disease duration (89).

An investigation of factors which could account for the difference in prevalence between ANC and the general population were assessed in two of the studies. Glynn et al found age, marital status, parity, education status and contraceptive use as important factors which might influence the differences in HIV prevalence in ANC and the population, however the importance of these factors varied between different cities (87). Crampin et al found age, area of residence, marital status and moving household within the last 5 years to be important factors, although parity did not account for any of the difference (86). These studies highlight the difficulties of applying standard adjustments for ANC data to population estimates across different cities.

A difficulty when comparing ANC and the general population is ensuring the two catchment populations of women are well defined and comparable. Attendance at antenatal clinics is variable and on a global basis it has been estimated that a third of women receive no antenatal care, although this proportion varies widely according to country (90). If some pregnant women in an area do not attend the antenatal clinic, and those who do not attend have a different prevalence of HIV from those who do attend, a bias would arise. ANCs may be more health conscious and have different socio-economic characteristics from pregnant women who do not attend. A different type of bias may have been that the studies reviewed here were carried out at various times over a number of years. As HIV first entered the different populations at different times, the epidemics will have reached different stages of maturity at the times of the studies. Therefore, the ratio of HIV prevalence in pregnant women to that in all women could vary with stage of the epidemic.

Finally, a health survey in Kenya collected demographic and HIV testing information on 9,000 households. Results revealed that women were more likely to be HIV-positive than men (9% versus 5%), the proportion of women found to be HIV-positive rose rapidly with age from 4% among 15-19 year olds to 12% in 25-29 year olds and that HIV prevalence derived from this population survey was similar to estimates observed amongst antenatal women (8.7% versus 9.4%) (91).

In summary, findings from these studies indicate that the prevalence in pregnant women may underestimate prevalence in the general population and this level of underestimate varies by age and area. These data are consistent with results presented in the previous section which found lower birth rates in HIV-infected individuals than in uninfected individuals. However, these findings apply to SSA and although they highlight possible biological and behavioural explanations, it is unclear to what extent the same associations hold in GB.

Table 2.3:Studies comparing HIV prevalence in antenatal clinics with HIV prevalence in the female population: Developing countries

Author, year Location	Kigadye, 1993 Mwanza, Tanzania	Kwesigabo, 1996 Kagera, Tanzania	Fylkesnes, 1998 Lusaka & Mposhi Zambia	Kilian 1999 Uganda	Glynn 2001 Cameroon	Glynn 2001 Kenya	Glynn 2001 Zambia	Changalucha 2002 Mwanza, Tanzania	Crampin 2003 Karonga, Malawi
Population survey prevalence (unadjusted)	15.1%	29.2%	L=29.9% M=17.4%	26.0%	7.8%	30.1%	31.9%	4.7%	17%
Population survey prevalence (adjusted)	-	29.4%	L=31.2%a M=17.4%a	-	7.7%b	31.1%b	32.7%b	-	13.9%
Prevalence in ANC (unadjusted)	11.7%	22.8%	L=26.1% M=12.6%	18.4%	5.5%	30.6%	27.3%	3.6%	10.4%
Prevalence in ANC (adjusted)	-	22.4%	L=24.4%a M=12.5%a	-	5.2%b	29.2%b	26.0%b	-	9.2%
No. of women in population survey	589	325	L=1211 M=426	527	1017	893	910	5675	342
No. of women in ANC attenders survey	1820	1292	L=532 M=422	477	1532	1480	1021	2265	3013
Year of survey	1990-91	Pop survey 1987-88 ANC survey 1990	Pop survey 1995/6 ANC survey 1994/6	1995	1997-1998	1997-1998	1997-1998	1991-1994	1998-2001
Age group	15+	15-54	15-39	15-49	15-40	15-40	15-40	15-44	15-49
Prevalence Ratio	**0.77**	**0.76**	**L=0.78** **M=0.72**	**0.71**	**0.68**	**0.94**	**0.80**	**0.77**	**0.66**

a. Standardised for age using the Zambian 1990 census population as projected for 1995 as standard population. b. Adjusted for age

2.4: Rates of reproductive events in HIV-positive women before and after diagnosis

In developed countries the effects of HIV infection on fertility has commonly been measured by comparing rates of reproductive events before and after HIV diagnosis in cohorts of positive women (Table 2.4). In the earlier studies, live birth rates decreased significantly after HIV diagnosis whilst termination rates increased (68,92-94). A French study published in 2001 showed that whilst pregnancy rates after HIV diagnosis decreased among European women, incidence of births increased among African women with fewer than 2 children, but not among those already having more than 2 children (95).

Stephenson et al compared the rates of reproductive events before and after diagnosis of HIV in a cohort of 503 HIV-positive women in Great Britain and Ireland in 1992-95 (68). For women aged 20-34, the age-adjusted livebirth rate fell by 44% from 10.2 per 100 women years before diagnosis to 5.7 per 100 women years after diagnosis. An increase in termination rates accounted for approximately half the decline whilst an increase in the miscarriage rate and a decrease in the pregnancy rate accounted for the other half. Similar decreases in incidence of pregnancy and increases in abortion were also reported by De Vincenzi (France), Thackway (Australia) and Van Benthem (Europe) (92-94). Similar to the findings of Fourquet, Stephenson et al also found HIV-positive women of African origin continued to have higher pregnancy rates than HIV-positive women of European background. A different study by Forysth showed that in a city in America pregnancy rates amongst HIV-infected women were lower when compared with HIV-negative women, although this decrease was more striking when the women's history of drug use was taken into consideration (96).

The incidence of pregnancy in a European study was also shown to decrease with HIV disease progression and pregnancies after HIV diagnosis were shown to be related largely to social and cultural attitudes (94). Pregnancy rates in Southern Europe were lower than in Central and Northern Europe and women living with a sexual partner were more likely to become pregnant after diagnosis than women without such a partner. A later study by Lee et al in the USA researched the effect of duration of infection with HIV on fertility by looking at the birth histories of women with AIDS and comparing them to uninfected women. The relative risk of giving birth in HIV-infected women was low compared to uninfected women and there was a clear negative gradient with duration of infection. These results suggested that HIV-infected women experience a progressive reduction in births years before the onset of AIDS. Demographic characteristics, contraception, induced abortion, fetal loss and illicit drug use could not explain the findings (97).

There has been a body of evidence early in the epidemic which suggested that HIV infection did not alter the likelihood of women becoming pregnant (67,98), nor did it affect the rates of either spontaneous abortions or planned terminations of pregnancy (65). The year the studies were carried out, the relatively small sample sizes used and the high proportion of drug users amongst the population groups under study may explain the discrepancy with the growing body of evidence that there is an effect.

Finally, two recent studies have compared pregnancy rates in HIV-infected women pre and post highly active anti-retroviral therapy (HAART), to determine whether improvements in HIV management have contributed to changes in pregnancy decision-making. Availability of treatments to delay HIV disease progression have made many HIV-infected women feel better which in turn may change their desire for future children. Effective interventions to reduce mother to child transmission (MTCT) have become widely available and the likelihood of an HIV-infected woman having an infected child is now very small. Finally it is not known what effect the introduction of routine antenatal HIV testing has had on pregnancy decisions. Increasing proportions of previously unidentified infected women are now having their infection diagnosed earlier than they would have otherwise and this may impact differently on both immediate and future fertility decisions.

A study by Massad et al compared pregnancy rates in a prospective study involving 2059 HIV-positive women and 569 HIV-negative women (99). The study was carried out in the USA between 1994 and 2002 and studied frequency and outcome of pregnancy both pre and post HAART. Whilst pregnancy rates were 7.4 and 15.2 per 100 person-years in seropositive and seronegative women respectively ($p<0.0001$), pregnancy outcomes were similar. The abortion rate of HIV-positive women fell about the time of HAART introduction while conception rates remained stable, suggesting that positive women who conceived were more likely to continue their pregnancies after HAART rather than HAART led women to conceive who would not otherwise have done so. Another study in the USA demonstrated modest increases in pregnancy rates during the era of HAART and the authors hypothesised that increased survival times for women with AIDS as well as delayed progression to AIDS may result in greater opportunities to become pregnant. Data on outcome of these pregnancies was however unknown (100).

In summary, studies in the developed world which have compared pregnancy rates before and after HIV diagnosis have shown overall decreases in live birth rates after HIV diagnosis, although this was dependent on the cultural background of the woman. Whilst results may suggest an association between HIV and fertility, a causal link was not demonstrated and little data were available on whether the association was related to decision-making, lifestyle factors such as loss of partner or was a biological phenomenon.

Table 2.4: Rates of reproductive events in HIV-positive women before and after diagnosis: Developed countries

Author, year	Stephenson, 1996	De Vincenzi, 1997	Thackway, 1997	Van Benthem, 2000[b]	Fourquet 2001[c]	Massad 2004[c]
Location	UK	France	Australia	Europe	France	USA
Live Birth Rate HIV positive (per 100 PY)	All: 5.7 Black African: 12.0 IDU: 5.0 Rest: 4.4	2.1	30 per 10,000[a]	8.2 (0-4 yr) 6.0 (+4 yr)	Black African:14.1 Other:4.5	7.4
Live birth Rate HIV negative (per 100 PY)	All: 10.2 Black African: 12.6 IDU: 11.0 Rest: 7.5	8.1	63.5 per 10,000[a]	8.6	Black African: 8.7 Other:5.3	15.2
Total no. HIV positive in study	503	412	294	449	533	2059
Fertility Ratio	**All:0.56** **Black African:0.95** **IDU:0.45** **Rest:0.59**	**0.26**	**0.47**	**0.95 (0-4 yr)** **0.70 (+4 yr)**	**Black African: 1.62** **Other: 0.85**	**0.49**
Date	1992-1995	1988-1993	1984-1994	1993-1998	1988-1996	1994-2002

[a]Pregnancy rate per 10,000 women. Control group were all Australian women aged 15-44 years.
[b] Live births, still births and spontaneous abortions
[c] Incidence of pregnancies per 100 person years

2.5: Other evidence

Many other studies have looked at the association of HIV and fertility and these include retrospective studies of pregnancy rates in HIV-positive women, studies on the incidence of pregnancies and studies looking at adverse effects of HIV on neonatal outcome and disease progression. Some studies investigate possible reasons for the observed associations.

2.5.1: Retrospective studies of pregnancy rates amongst HIV-positive and HIV-negative women

In 1995-6 a retrospective study involving 4,369 women (530 of which were HIV-positive) was carried out in Abidjan, Cote d'Ivoire to determine the differences in fertility between HIV positive and negative women (101). The mean number of pregnancies for the HIV positive compared to the HIV-negative was significantly greater for women aged under 20 but significantly lower for HIV-positive women aged 25-34 years. HIV infection was also significantly associated with a higher risk of abortions (spontaneous and induced combined) and stillbirths. As all women were unaware of their infection status, results were unlikely to have been influenced by a change in reproductive behaviour and this study therefore suggests HIV has deleterious consequences on fertility. A later study by the same investigators, which collected more detailed information on fertility history, found that the interval between the last pregnancy and the current pregnancy was considerably longer among infected women (102). This supports the author's previous hypothesis that HIV lowered fertility among infected women in terms of their ability to become pregnant.

2.5.2: Incidence of pregnancies amongst HIV-positive women

A study of the incidence of pregnancy was carried out after HIV testing and counselling in Kigali, Rwanda in 1998 (103). A population-based sample of 1,458 women aged 18-35 (460 HIV-positive and 998 HIV-negative) of known HIV status was followed for two years. At the initial survey, 11% of the HIV-positive women were pregnant compared with 17% of the HIV-negative. Even though HIV-negative women were significantly more likely to become pregnant in the 2-year follow-up period than HIV-positive women (58% vs. 43%), the incidence of pregnancy in HIV-positive women was still high. This relationship persisted after adjusting for age, marital status and frequency of intercourse.

Rather than compare HIV-positive and negative women, groups which may differ on various sociodemographic and behavioural characteristics, other researchers in the USA have not used a control group and have studied directly the pregnancy incidence in women who were aware of their HIV seropositivity (104-106). These studies have explored factors which may intervene in fertility decisions. Nebie et al showed that in a cohort of HIV-positive women who were followed for up to four years, pregnancy incidence was comparable with that in the general population. Sharing of the HIV test result with the male sexual partner was however infrequent and contraceptive use was low. Kline et al (105) found that a woman's reproductive history was important to her current reproductive behaviour, whereby women who became pregnant knowing their positive status had experienced more previous pregnancies than other women.

2.5.3: Effect of HIV on neonatal outcome

Several studies have investigated the impact of HIV infection on adverse neonatal outcome. This is a critical issue which has major implications for HIV-positive women who are considering becoming pregnant. Table 2.5 shows the main results from these studies which have been carried out in both developed and developing countries. In many studies, there was an increase in risk of miscarriage among HIV-infected women compared with HIV-negative women, with reported Relative Risks or Odds Ratios (RR and OR) varying from 1.7 to 3.4 (65,102,107-109). This difference was not however always statistically significant. Some studies have found an RR/OR of greater than 1, varying from 1.3 to 3.1, but with 95% CI including 1 (67-68,92,110-112). Only two studies have calculated an RR/OR of spontaneous abortion that was less than 1.0 (75,98). Possible reasons for an adverse effect on neonatal outcome include a direct effect of HIV on the placenta, thymic abnormalities, altered cytokine production and the cumulative immunosuppressive effect of HIV that may have a role in facilitating ascending infection (107). Women with HIV were also more likely to have a history of STIs (78) and infection with syphilis is a known cause of fetal loss (113).

In a meta analysis of these studies, Brocklehurst and French reported that a modest relationship was found between HIV infection and fetal loss (114). However, they suggested that these findings might have resulted from inadequate adjustment for confounding variables and biases associated with study design. Women infected with HIV may have a higher incidence of STIs and, in developed countries, a higher incidence of past or current drug use. Observational studies are prone to bias insofar as the two groups compared (ie. HIV-positive and HIV-negative women) may be dissimilar in other characteristics apart from their HIV status. Further large prospective cohort studies which attempt to control for confounding were therefore recommended to more accurately define the effect of HIV on spontaneous abortion.

A few studies have also looked at stillbirths as an outcome of pregnancy. A review of these studies concluded that there appeared to be no association between HIV infection and stillbirth in developed countries, although the total numbers of women included in the surveys was small (114). In developing countries there was statistically significant evidence that the risk of stillbirth was increased (summary OR 4.15, 95% CI 2.81-6.15), although this could now change in the era of HAART.

Table 2.5: Review of literature on HIV infection on adverse pregnancy outcome*

Author & Year	Country	Study design	No. HIV positive	No. HIV negative	% spontaneous abortion	% stillbirth	Risk Abortion[7]	95% CI[8]	*P* value[8]
Johnstone 1988	Scotland	Prospective	61[1]	75[1]	18.0 vs 5.3	-	RR3.4	NR	<0.02
Selwyn 1989	USA	Prospective	52[2]	73[2]	7.7 vs 5.5	0 vs 0	RR1.4	NR	NR
Ryder 1991	Africa	Prospective	197[2]	295[2]	52.1 vs 51.6[4]		RR0.62	NR	NR
Sunderland 1992	USA	Prospective	37[1]	37[1]	5.4 vs 8.1	-	RR0.67	NR	NR
Stephenson 1996	UK	Prospective	202[3]	580[3]	16.0 vs 10.0	-	RR1.6	NR	NR
De Vincenzi 1997	Europe	Prospective	84[3]	110[3]	25.4 vs 8.3	-	RR3.1	NR	NR
Braddick 1990	Africa	Retrospective	177[2]	327[2]	11.0 vs 8.0	3.0 vs 3.0	RR1.4	NR	NR
Miotti 1990	Africa	Retrospective	64[2]	311[2]	28.1 vs 15.1	-	OR2.2	NR	NR
Temmerman 1994	Africa	Retrospective	281[2]	275[2]	7.8 vs 3.6	3.8 vs 1.9	OR2.0	0.9-4.8	0.1
De Cock 1994	Africa	Retrospective	839[1]	1220[1]	7.3 vs 5.7	3.0 vs 2.1	RR1.3	NR	NR
D'Ubaldo 1998	Italy	Retrospective	175[2]	97[2]	14.3 vs 9.6	-	RR1.7	0.71-3.92	0.24
Desgrees du Lou 1999	Africa	Retrospective	169[1]	1013[1]	0.21 vs 0.17[5]	-	RR1.2	NR	0.38
Coley 2001	Africa	Prospective	520[2]	485[2]	3.3 vs 2.3[6]	6.5 vs 6.4	RR1.4	NR	0.34

[1] Number of pregnancies studied [2] Number of women studied [3] Number of pregnancies in same group of women before and after diagnosis
[4] Incidence rate [5] Mean number of miscarriages [6] Percentage of miscarriages as outcome of current pregnancy
[7] RR=Relative Risk and OR=Odds ratio [8] NR=Not recorded
*Adapted from D'Ulbado et al (107) and updated with recent studies. Data on stillbirths has been additionally included.

2.5.4: Effect of pregnancy on progression of HIV disease

The effect of pregnancy on the natural history of HIV disease is an important factor when counselling HIV-positive women considering pregnancy. Concerns regarding a possible interaction between pregnancy and HIV disease progression stemmed from early reports of an association between HIV infection and deteriorating maternal health (115-116). Both studies found that a certain proportion of HIV-infected pregnant women experienced clinical progression. However, these studies lacked a control group, and it is likely that the HIV-positive women who were enrolled were more immunosuppressed, given that they were identified via recognition of HIV infection in their infants. These studies were, however, suggestive and inspired future work in this area.

Subsequent findings from prospective studies suggested that pregnancy does not affect early progression of HIV disease (117-118). A review of seven prospective studies in 1998 did not find significant differences in the risk of death or progression to an AIDS-defining illness, although there were trends suggestive that there may be a weak association between disease progression and maternal outcome of HIV-infected women. Studies reviewed involved relatively small numbers of women making it impossible to determine with any certainty the effect of pregnancy on HIV disease progression and survival (119).

Finally, some studies have looked at the impact of pregnancy on T-cell lymphocyte populations as a measure of immuno-function decrease. Data from the European Collaborative Study and the Swiss HIV Pregnancy Cohort did not find decreases in CD4 cell count percentages throughout pregnancy and up to 6 months after delivery

(120). In a more recent European study whilst pregnancy was shown not to have a statistically significant effect on CD4 lymphocyte counts, median levels pre and post pregnancy suggested a temporal decrease (121). It is difficult to determine how important this is to HIV disease progression.

2.5.5: Effect of Sexually Transmitted Infections on infertility

It is well established that STIs can cause infertility, and that infertility can lead to high risk behaviour and HIV infection (79). This is of particular importance in SSA where the prevalence of infertility is high and in the monitoring of the HIV epidemic as the inability to become pregnant affects estimates of HIV prevalence amongst ANC. The association of HIV infection and fertility has been investigated by recruiting women from either infertility or abortion clinics. A study by Favot in Tanzania between 1994 and 1995 showed women attending an infertility clinic had a higher HIV prevalence than women proceeding to birth in the same hospital (18.2% v 6.6%) (122). This was also shown in a study by Schrijvers where infertile women had a HIV prevalence of 9.3% whilst fertile women had a HIV prevalence of 0.7% (123). The authors hypothesised that the higher prevalence of HIV in the group of infertile women could reflect the higher level of STIs in this group with the associated higher risk of HIV infection.

2.5.6: Factors associated with reproductive-decision making amongst HIV-positive women

Finally, some studies have looked at factors associated with pregnancy-decision making in cohorts of HIV-infected women, some before and some after improvements in HIV-related therapy. All these studies have been undertaken in America (105-

106,124-126) or the UK (127) and found that an appreciable number of infected women desired children and this was associated with factors such as age, marital status, partner's desire for children, partner's HIV status and personal health status. Ethnic differences in the desire for children were apparent (127). In summary, the studies showed that women with HIV do not rule out childbirth, although decisions surrounding their pregnancies are complex.

2.6: Key Points

1. A substantial body of evidence exists which indicates that HIV-positive women have a lower fertility ratio than HIV-negative women in developing countries (OR 0.73-0.81) and in developed countries HIV-positive women were found to have a lower live birth rate post HIV diagnosis compared to pre HIV diagnosis (OR 0.26-0.95)
2. A number of studies have assessed how well HIV prevalence among pregnant women reflects prevalence in the general population and have found the ratio of HIV prevalence in pregnant women to HIV prevalence in all women ranged from 0.66-0.94.
3. A number of possible reasons for reduced fertility amongst HIV-positive women have been suggested; Avoidance of pregnancy to prevent onward transmission to a partner or child or to avoid orphanhood; an effect of HIV on fecundity; increased adverse outcome of the neonate due to HIV infection or other STIs.
4. Since the majority of the studies in the developed world were carried out, improvements in the management of HIV have occurred and it is not known how this may have affected reproductive decision-making amongst HIV-positive women.
5. Although important understanding has been acquired regarding the association between pregnancy and the course of HIV infection, much remains to be understood. Whilst a fertility differential between HIV-positive and HIV-negative women does not invalidate neonatal seroprevalence monitoring, it does indicate that extrapolations of seroprevalence from pregnant women to

all women should be cautious and methods to overcome the fertility bias should be developed.

Chapter 3: Aims, Objectives and Data Sources

3.1: Aims and objectives

The aim of this thesis is to develop a model to estimate the number of HIV infections amongst women in the general population using neonatal seroprevalence data. The objectives are as follows:

1. To assess the bias of differential fertility patterns between persons at high and low risk of HIV when producing general population estimates and to determine the important factors associated with fertility and HIV risk (Chapter 4).

2. To assess current fertility patterns in diagnosed HIV-infected women and to explore the impact of improved antenatal testing, and possible earlier diagnosis, on pregnancy outcome (Chapter 5).

3. To assess whether fertility decisions amongst HIV infected women have changed due to increasing availability of treatments and interventions and how any changes would have affected trends in seroprevalence data (Chapter 6).

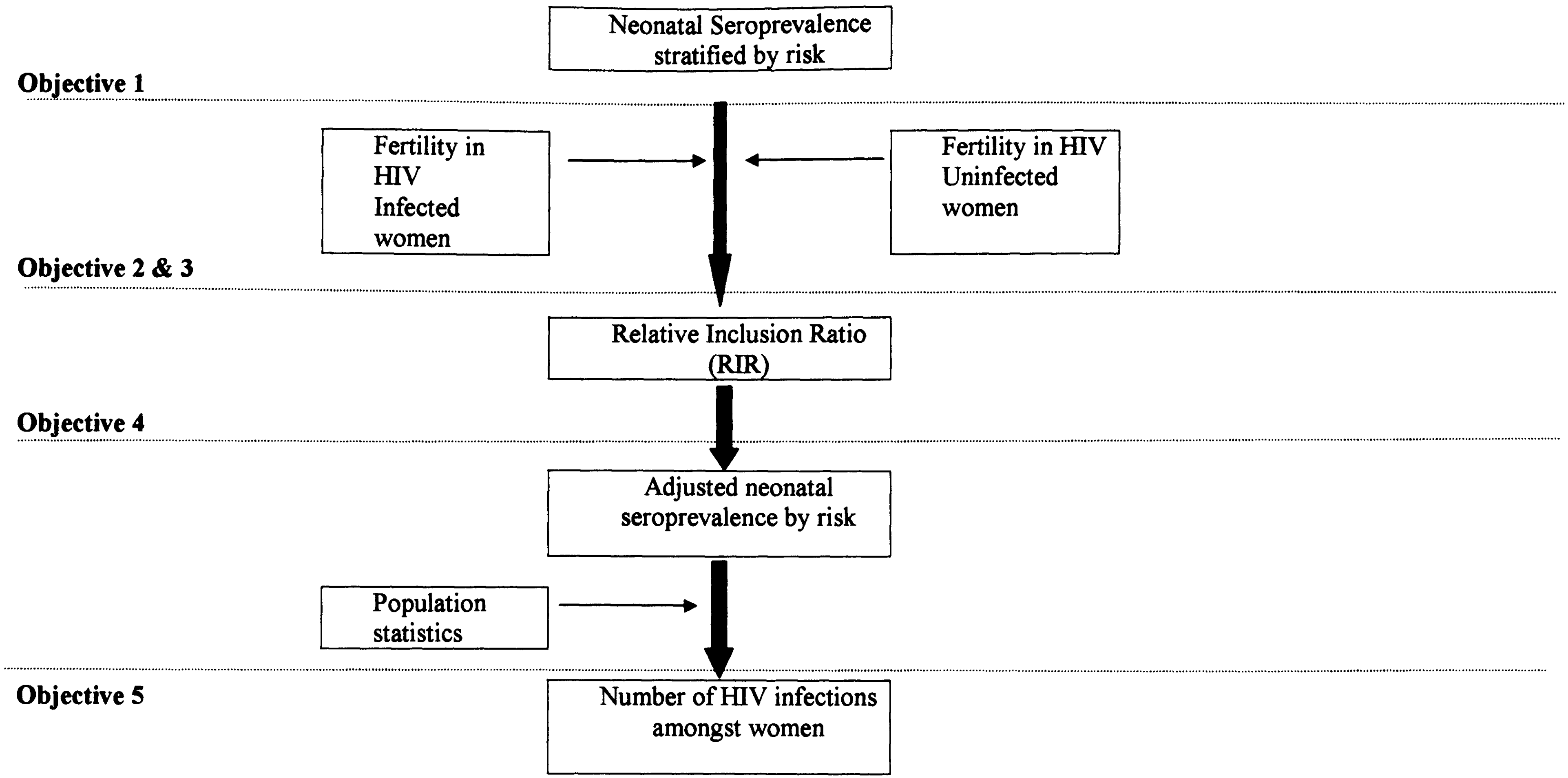
4. To estimate the Relative Inclusion Ratio (fertility differential) between HIV-positive and HIV-negative women, using results obtained under objectives 1 and 3 (Chapter 7).

5. To define, use and validate a model to adjust neonatal seroprevalence so it reflects HIV prevalence in the general population. Data derived from

objectives 1-4 will be used to help formulate this model. The adjusted neonatal prevalence will then be applied to population statistics to derive the number of HIV infections amongst women (Chapter 7).

To address these objectives a variety of different data sources were used. A cross-sectional questionnaire survey investigating the impact of an HIV diagnosis on fertility desire was carried out specifically for the purpose of this thesis. In addition, routine data containing information on HIV prevalence in pregnant women, reports of newly diagnosed HIV-infected women, prevalence of diagnosed HIV infections and reports of HIV-infected pregnant women were extracted from data sources at the HPA Communicable Disease Surveillance Centre (CDSC) and the Institute of Child Health (ICH). Finally, 2001 census information, birth statistics and information from the 2001 National Study of Sexual Attitudes and Lifestyles (NATSAL) were used to supplement analyses. All this information was then put together to generate the final model which adjusts neonatal seroprevalence data (Figure 3.1). A table summarising the different data sources used is given at the end of this section (Table 3.2). Results from objective 1 were published in Communicable Disease and Public Health in March 2004 (Appendix A).

Figure 3.1: Approach for adjustment of neonatal seroprevalence data to all women



3.2: Questionnaire survey to assess impact of HIV on fertility-decision making amongst women

3.2.1: Study design

Previous research has shown an association between HIV and fertility, although little information has been gathered on factors which would help explain this relationship. For these reasons a cross-sectional questionnaire survey was undertaken for the purposes of this thesis in order to improve our understanding of reproductive-decision making amongst HIV-infected women. The design of this survey enabled the women to be directly asked themselves about their desires for children. It was important that the data collected were from a representative sample of HIV positive women and that enough women were included in order for the data to be robust enough to be included in the final model of the thesis. The aims and objectives of this study are described in detail in chapter 6.

All HIV-positive women of reproductive age (16-49 years) who were attending one of the participating HIV clinics during the time period of the study were asked to complete a questionnaire whilst waiting for their clinic appointments. Questions were semi-qualitative and the form was self-completed by the women, usually whilst waiting for clinic appointments (Appendix B1). An information sheet was given to all women prior to the completion of questionnaires and women agreeing to participate in the survey were asked to sign an informed consent form (Appendix B2 and B3). The choice of taking the questionnaire home for completion was given and the questionnaire was available in French as well as English. After completion of the questionnaire a Boots voucher was given to the women as a thank you. For those women declining to complete the whole form, basic demographic details (age, residence, ethnicity, parity and reason for declining) were requested to inform assessment of potential bias.

During the development phase of the survey, comments on the questionnaire (in terms of topics covered and format) were received and incorporated from a variety of relevant researchers within ICH and CDSC. Prior to the study commencing, the questionnaire was piloted on 10 women at Great Ormond Street Hospital and 5 women at the voluntary organisation Positively Women. During the pilot phase the appropriateness of the questions was assessed. In addition, issues of confidentiality were assessed prior to the study commencing. No personal identifying information was requested on the questionnaire. Whilst subjects were asked to complete a signed consent form prior to completion of the questionnaire, the consent forms were stored separately in a locked cabinet within clinic. With the exception of Manchester, the survey only took place during clinics specifically organised for HIV positive individuals. As Manchester did not have any exclusive HIV clinics, patients from that centre were asked to complete the questionnaire at home. All women were approached sensitively and were given the option of not participating in the survey or taking the questionnaire home for completion.

Ethics approval was obtained from the London Multi-Regional Ethics Committee (reference 03/2/023 April 2003) and the ethics committees of all institutions involved in the study, including Great Ormond Street Ethics Committee which was the main research institution of the study.

3.2.2: Study sites

To ensure a representative sample of HIV-infected women were included in the survey, numbers of HIV-positive women currently receiving care by treatment centre and risk category was obtained using data from the Survey of Prevalent HIV Infections Diagnosed (described in section 3.7) and used to select the HIV clinics in Great Britain which participated in the survey. Clinics were selected in areas of relatively high prevalence of HIV infection amongst women, with a substantial number of HIV-positive women on their case load. After each clinic was personally invited to participate in the survey, meetings took place to establish logistics and local research teams.

Seven of the eight HIV specialist clinics contacted were included in the study: St Mary's Hospital (London), Newham General Hospital (London), Chelsea & Westminster Hospital (London), Nottingham City Hospital, Leicester Royal Infirmary, North Manchester General Hospital and Western General Hospital (Edinburgh). In addition, women were also recruited from two voluntary organisations in London (London East AIDS Network (LEAN) and Positively Women) and the family clinic at Great Ormond Street Hospital. The eighth clinic contacted declined to participate as it was felt the patients had already recently taken part in other research projects. A list of collaborators is detailed in Appendix C.

3.2.3: Sample size and power calculations

It was anticipated that the selected clinics would see approximately 1000 women during the survey period (ranging from 40-350 per clinic). Recruitment of 400 women (300 black African and 100 Rest) was considered to be within the survey resources and this was based on the recruitment of 100 women per London centre and 25-50 women per outside London centre, and knowledge about their HIV risk. A similar type of questionnaire survey was carried out recently in London which had a 65% acceptance rate (128), and we hoped to achieve at least that in this epidemiological study in order to reduce any participation bias.

The statistical power of the survey based on recruitment of 400 women was assessed prior to implementation. Power calculations were explored focussing on questions 27 and 28 from the questionnaire, which were central to the research and assessed whether or not improvements in HIV management had changed women's reproductive decisions. As there had been little previous research in this area the proportion of affirmative responses for each of our sub-groups of interest was based on a range of hypothetical values (0.5, 0.25, 0.15 and 0.05). It was found that a likely scenario would require differences between the proportions for Africans and Rest of 6.8% and 15.6% to achieve a significant result with 80% power and 5% significance level for one-sided comparisons. The actual number of participants in this study was 450 women.

3.2.4: Data collection

Data were collected between May 2003 and January 2004 (Table 3.1). The structured questionnaire focussed on demographic factors, HIV test history, pregnancy history and desire for more children. At the end of the questionnaire a comments section was included which requested further information on any additional factors which may have influenced pregnancy decision-making, including partner's feelings, asylum status and financial situation. This information was entered onto the computer and analysed as free text.

Table 3.1: Recruitment period of clinics involved in the survey

Clinic	Start date	End date
Great Ormond Street Hospital (Pilot)	May 2003	May 2003
Positively Women (Pilot)	May 2003	May 2003
St Mary's Hospital (London)	July 2003	September 2003
Newham General Hospital (London)	August 2003	October 2003
Chelsea & Westminster Hospital	October 2003	January 2004
Leicester Royal Infirmary	July 2003	October 2003
Nottingham City Hospital	August 2003	January 2004
Western General Hospital (Edinburgh)	October 2003	January 2004
North Manchester General Hospital	November 2003	January 2004
London East AIDS Network (LEAN)	September 2003	September 2003

3.3: Unlinked Anonymous HIV Prevalence Survey amongst Newborns

The prevalence of HIV infection among pregnant women in GB is monitored through three surveys within the unlinked anonymous (UA) programme, the dried blood spot survey, the antenatal clinic attenders survey and the termination of pregnancy survey (23). Only the first two of these surveys will be used for the purposes of this project as women in the termination of pregnancy survey were not expected to be representative of women in the general population. Overall HIV prevalence amongst pregnant women includes those with previously diagnosed infections, those diagnosed through antenatal screening and those remaining undiagnosed at delivery.

The Dried Blood Spot survey (DBS) tests residual neonatal dried blood spot samples from Guthrie cards used for the screening of infants for metabolic disorders (6). The blood sample, which is usually taken by a midwife during the neonates first week of life, is blotted and dried on a Guthrie card which includes demographic information about the mother and child. Since maternal antibodies cross the placenta, the neonate's antibody status serves as a measure of maternal status with respect to HIV (129). The surveys began in 1988 and cover Scotland and the former Thames (which includes London), West Midlands, North Western, Mersey and Trent regions. In 2002 over 450,000 dried blood spots were anonymously tested for HIV, representing 70% of all live births in GB that year (23).

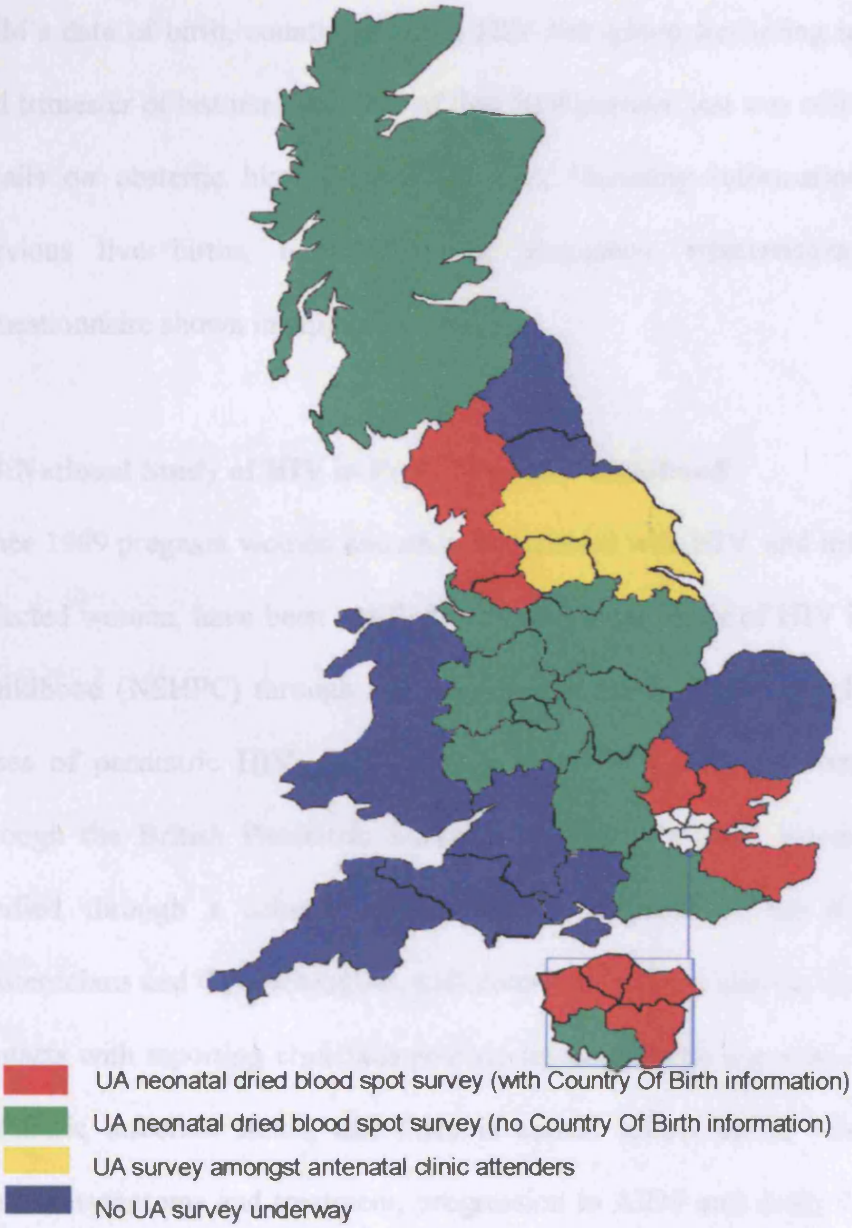
Since a criterion of the UA programme is that patients must be informed that their samples may be used in the surveys though posters and leaflets, some women may object to their samples being used and these are then excluded from the surveys. Some residual samples (ie. What is left of the sample after it has been used for the purpose it was originally taken) may also be excluded if they are of insufficient volume for testing. Objection rates and numbers of insufficient samples are continuously monitored and are usually less than 1%. In addition to a sample not being available for UA testing, it has been estimated that 4% of infants may not have received routine neonatal screening and would therefore not be included in UA testing (63). Whilst non-screened infants were found more likely to be black African, it was not thought this would represent a bias to the DBS survey (62).

All regions participating in the DBS survey collect data by area of residence (provider code pre-1992). However, between 1997-2000 the survey was enhanced in 3 areas (former North Thames, South East Thames and North Western Regions) to include linkage of birth registration data and information from the child's Guthrie card to dried blood spots prior to anonymisation (29,55). This enhancement enabled the collection of additional information for the mother, including country of birth and age. In 2002 approximately 40% of samples (and all samples in North and South East London) collected though the DBS survey were covered by this linkage facility.

The UA antenatal survey tests left over blood samples taken at antenatal clinics for rubella serology. Data on age group is collected but not details on country of birth. Antenatal surveys began in 1990 in three regions, Thames, Yorkshire and North Western. Surveys in the first two regions are on-going, but the one in North Western ended in 1992. As data from Thames is also included in the DBS survey, only the Yorkshire data has been included in this project. Results of HIV prevalence amongst women receiving antenatal care were assumed to be the same as that amongst women proceeding to live birth.

For areas not participating in the UA surveys, prevalence estimates amongst women with live births were obtained based on a regression of the proportion of seropositives against data on the number of diagnosed women in districts of residence participating in the UA surveys. The latter data were collected in the Survey of Prevalent HIV Infections Diagnosed (SOPHID) (130). The fitted regression equation is applied to SOPHID data to generate prevalence estimates in areas not covered by UA testing. Figure 3.2 shows geographical coverage of the DBS survey, enhanced DBS survey and the antenatal clinic attenders survey. The UA annual report provides further details about these surveys (23).

Figure 3.2: Coverage of UA surveys which monitor HIV seroprevalence amongst pregnant women in GB



3.4:European Collaborative Study

The European Collaborative Study (ECS) is a prospective cohort study of children born to HIV infected mothers in 26 centres throughout Europe (35). At participating centres, all pregnant women are screened for HIV infection and those found to be infected are invited to participate in the study. Information on mother's date of birth, child's date of birth, country of birth, HIV risk group (including injecting drug use and trimester of last use) and date of first HIV positive test was collected. In addition details on obstetric history were gathered, including information on number of previous live births, terminations of pregnancy, miscarriages and stillbirths. (Questionnaire shown in Appendix D).

3.4:National Study of HIV in Pregnancy and Childhood

Since 1989 pregnant women known to be infected with HIV, and infants born to HIV infected women, have been notified to the National Study of HIV in Pregnancy and Childhood (NSHPC) through two confidential active reporting schemes (24). New cases of paediatric HIV, and infants born to HIV infected women, are reported through the British Paediatric Surveillance Unit. Pregnant women with HIV are notified through a scheme run under the auspices of the Royal College of Obstetricians and Gynaecologists. Laboratory reports are also incorporated. Repeated contacts with reporting clinicians provide information on outcome of pregnancy and paediatric infection status, and there is annual follow up of infected children to monitor symptoms and treatment, progression to AIDS and death. Names of women and children are not sought or recorded, but reports are linked using date and place of birth.

The obstetric scheme has had a response rate in excess of 95% since 1998 (131) and the paediatric scheme consistently reports a response rate in excess of 92% (132). It is not known how many women are diagnosed but not reported by the units who do not respond to the scheme, but multiple source ascertainment and repeated contact with respondents who fail to return their reporting cards is believed to keep this to a minimum. The effect of reporting delay has been monitored, and although there is considerable local variation in promptness of reporting, very few reports are made more than one year in arrears. The number of reported pregnancies diagnosed prior to delivery in 2002 is unlikely to increase substantially (Questionnaire shown in Appendix E).

3.6: Voluntary reports of newly diagnosed HIV infections

Voluntary confidential reports of new HIV diagnoses are received from laboratories and additionally since 2000, from clinicians (18). Date of birth, probable route of exposure, country of birth and parity are collected for all clinician reports. New AIDS diagnoses are reported by clinicians using the European AIDS case definition (133). Deaths occurring in HIV-infected individuals are reported by clinicians or ascertained through indirect matching with Office for National Statistics (ONS) death records. Since the beginning of 2000 information on previous live births have been included on the HIV infection reports in anticipation of this project.

3.7: Survey of Prevalent HIV infections diagnosed

The Survey of Prevalent HIV Infections Diagnosed (SOPHID) provides the number of individuals living with diagnosed HIV infection in E, W& NI. At the beginning of each year, all centres providing statutory health care for individuals with diagnosed HIV infection are asked to submit information on all those patients seen for care in the previous year (134). Information collected includes gender, area of residence, ethnic grouping, probable exposure, age, most advanced clinical stage of illness and level of antiretroviral therapy. The data reflect numbers of persons currently receiving HIV-related treatment, whereas the voluntary confidential HIV reports include all people diagnosed with infection and will include persons who have subsequently died or who have maybe left the country. Numbers of prevalent diagnosed HIV positive women receiving care in Scotland was obtained from CD4 surveillance, a measure of the number of women who had undergone immunological testing for their HIV infection in the previous year (135).

3.8: Census of England & Wales and Scotland

The census is a population survey legally required to be answered by everyone and is carried out every 10 years. It is the most complete source of information about the population that we have in GB. The last census was carried out in 2001 and includes information on age, residence, country of birth and ethnicity.

Data from the census has been made available by ONS (England and Wales) and General Register Office (GRO) (Scotland) in the form of excel spreadsheets and these tables have been used to estimate the numbers of persons born in SSA and Rest of the world by current area of residence in GB. The definition for SSA was taken from the United Nations Classification of Countries by Development Region and Geographical area and consisted of Eastern Africa, Middle Africa, Southern Africa and Western Africa (136).

3.9: Birth Statistics

Information is collected at civil registration of every birth (unpublished, ONS (England) and GRO (Scotland)) and information requested includes age of mother, date of child's birth, area of residence and mother's and father's country of birth. An extract containing number of live births to women according to country of birth, age group and residence for 2002 was obtained from ONS and GRO.

3.10: National Survey of Sexual Attitudes and Lifestyles

The National Survey of Sexual Attitudes and Lifestyles (NATSAL) is a population survey carried out between 1999-2001 on a random sample of 4,762 men and 6,399 women aged 16-44 years, resident in GB. The survey provides estimates of patterns of sexual behaviour at the turn of the millennium, based on computer-assisted interviewing methods. One of the principal aims of NATSAL was to improve our understanding of HIV & STI epidemiology and in informing the development of future public health strategies in the field of sexual health. Topics included personal background, family, sexual experience, attitudes and lifestyle. The response rate was 63.1% (137). A stratified sample of addresses was selected, using a multistage probability cluster design with over-sampling in Greater London, where prevalence of risk factors was thought to be higher. The data were then weighted to adjust for the unequal probabilities of selection. In addition to the main study, a focussed study among Britain's ethnic minorities was undertaken to enable reliable analyses across ethnic groups.

A reduced dataset from NATSAL, containing the variables relevant to this project, was obtained from the Centre for Infectious Disease Epidemiology at the Royal Free and University College Medical School. A proposal for the analyses for this thesis were reviewed by the NATSAL project team. The dataset was received as a STATA file and all analyses were performed using the complex survey functions of STATA.

3.11: Role of the Researcher

Over the last 8 years I have been involved in the Unlinked Anonymous HIV Prevalence Surveys amongst Pregnant Women, carried out at both CDSC and ICH. I was the survey co-ordinator of the UA DBS survey between 1996 and 2000 and during that time developed the surveys in order to collect more detailed demographic data, results of which have been extensively used throughout this thesis. Between 2000 and 2004 I carried out the project presented in this thesis as part of an MRC training fellowship, whilst at the same time maintaining an advisory role on the UA programme. I conceived the idea and objectives of the project, together with my supervisors at ICH and CDSC.

I was the main investigator for the cross-sectional questionnaire survey to examine fertility-decisions amongst HIV-positive women (chapter 6). This involved development of the protocol and questionnaire, ethics approval, identification of collaborators, meetings with local investigators, survey co-ordination across all local sites, data collection in the London clinics, data management and data analysis. Results from this survey have been presented at the British HIV Association Conference April 2004.

The data analysed in chapters 4 and 5 were provided to me by epidemiologists at CDSC and ICH. I was given the responsibility for the analysis of the data, with the aim of clarifying the patterns of HIV risk and fertility amongst women in GB. The modelling work carried out in chapter 7 was developed and undertaken by myself. The direction and nature of the analyses were agreed in consultation with my supervisor, Professor Marie-Louise Newell, and co-supervisor Dr Mario Cortina-Borja.

Table 3.2: Data sources used in the analyses

Data Source	Information provided	Coverage	Objectives to which data contributed
Unlinked Anonymous (UA) neonatal dried blood spot survey	a) HIV prevalence amongst pregnant women proceeding to birth by residence, age and country of birth b) HIV prevalence amongst pregnant women proceeding to birth by residence	a) Former N Thames, SE Thames & North Western regions b) Former SW Thames, Eastern (part), Trent, Mersey, West Midlands & Scotland	Objective 1 & 5
Unlinked Anonymous (UA) antenatal clinic attenders survey	HIV prevalence amongst women receiving antenatal care by age & residence	Yorkshire	Objective 1 & 5
Cross-sectional questionnaire survey to monitor impact of HIV diagnosis on fertility decisions	Demographic data, HIV test history, fertility history and fertility desire for HIV-infected women	7 clinics and 2 voluntary organisations in England and Scotland	Objective 3 & 4
Survey of Prevalent HIV Infections Diagnosed (SOPHID)	Numbers of HIV-infected women receiving care by residence	England, Wales and Northern Ireland	Objective 2, & 5
Reports of newly diagnosed HIV infections	New reports of HIV-infected women by COB, age, parity, country of previous live births and year of previous live births	United Kingdom	Objective 2 & 4
National Study of HIV in Pregnancy & Childhood	Reports of HIV-infected pregnant women by residence, COB, parity, age, IDU history and timing of diagnosis (pre, during or after antenatal care)	United Kingdom & Eire	Objective 1, 2, 4 & 5
European Collaborative Study	Reports of HIV-infected pregnant women by country of residence, COB, parity, age and IDU history	26 centres in Europe	Objective 1, 2 & 4
NATSAL	Ethnicity, COB, age, residence, marital status, fertility history	Great Britain	Objective 2 & 4
Birth Statistics	Numbers of live births by residence, age group and COB	United Kingdom	Objective 1
Population Census	Numbers of women resident in the UK by residence, age and COB	United Kingdom	Objective 1 & 5

Chapter 4: The importance of differential fertility between women at high and low risk of HIV infection on interpretation of neonatal seroprevalence data

4.1: Introduction

Whilst seroprevalence data amongst pregnant women have been used to provide estimates of HIV-infected people in Britain (4-5), overall HIV prevalence in the general heterosexual population is unlikely to be similar to the unadjusted seroprevalence amongst pregnant women in areas with substantial adult populations from Africa (7). Women born in Africa who are resident in GB experience higher fertility than women born in the UK (8). These same women are also at increased risk of being HIV-infected (18). Injecting drug users are another sub-group of the population at increased risk of HIV infection but little is known about their fertility patterns. In the absence of published fertility data, previous estimates of persons in the general heterosexual population may have been biased upwards (4).

In order to derive more accurate estimates of HIV infection among the general population, this chapter explored the bias associated with differential fertility patterns in population sub-groups in GB at different risk of HIV and highlights the demographic factors which should be included in any adjustment model. The population was categorised into the three main groups of women at varying risk of HIV infection; women born in Sub-Saharan Africa (SSA), injecting drug users (IDUs) and women without either of these factors ('Rest') (18). Firstly, HIV risk amongst our sub-groups of interest were derived using neonatal seroprevalence data. As fertility rates in our population sub-groups are not published, routinely available population and births data from the Office of National Statistics (ONS) (England and Wales) and

General Register Office (GRO) (Scotland) and behavioural data from the National Study of Sexual Attitudes and Lifestyle (NATSAL) were analysed. Finally, as population and behavioural data on IDUs were limited, fertility information was supplemented with data gathered from a European prospective cohort of HIV-infected pregnant women (ECS). The number of drug using women participating in the ECS is high due to the inclusion of centres in Southern Europe, an area of the world with a relatively high prevalence of drug use. All data sources used in this analysis were described in detail in chapter 3.

4.2: Estimate of HIV risk amongst women

HIV prevalence for the sub-groups of women aged 16-44 years were estimated using neonatal seroprevalence data (50). Separate estimates were obtained for three geographical areas (London, Scotland and the Rest of GB) and four age groups (<20, 20-24, 25-29 and >=30) to allow for differences in fertility and HIV risk between these categories.

Information on country of birth was collected in some areas (predominantly South East including most of London) where unlinked anonymous (UA) testing was taking place. However, as no information on injecting drug use was retained with the prevalence data, the distribution of HIV by population category was supplemented using reports of diagnosed HIV-infected pregnant women received through the National Study of HIV in Pregnancy and Childhood (NSHPC) with number of live births for that year (24).

For areas not participating in the UA surveys, estimates were obtained either using UA data amongst ANC (Yorkshire) or they were based on a regression of the proportion of seropositives against data on the number of diagnosed women in districts of residence participating in the UA surveys (as described in chapter 3). The latter data were collected in the Survey of Prevalent HIV Infections diagnosed (SOPHID). The fitted regression equation was then applied to SOPHID data to generate prevalence estimates in areas not covered by UA testing. A high correlation coefficient (measure of association between SOPHID and UA data), R=0.98, was found for the fitted regression.

UA surveillance indicated that in 2002 the overall neonatal prevalence of HIV infection was 0.38% in London, 0.058% in Scotland and 0.050% in the rest of GB (Table 4.1). HIV seroprevalence by Strategic Health Authority (England), Scotland and Wales in 2002 is shown in Figure 4.1. Within London, prevalence ranged from 34 to 45 per 10,000 pregnant women. Outside London prevalence varied substantially from 1.8 in Yorkshire to 16.6 in Bedfordshire and Hertfordshire. In Wales and Scotland prevalence was 3.3 and 5.8 per 10,000 pregnant women respectively. These ranges in prevalence largely reflect the uneven distribution of African women resident throughout GB. Figure 4.1 also indicates whether or not a UA survey was being undertaken for each local area.

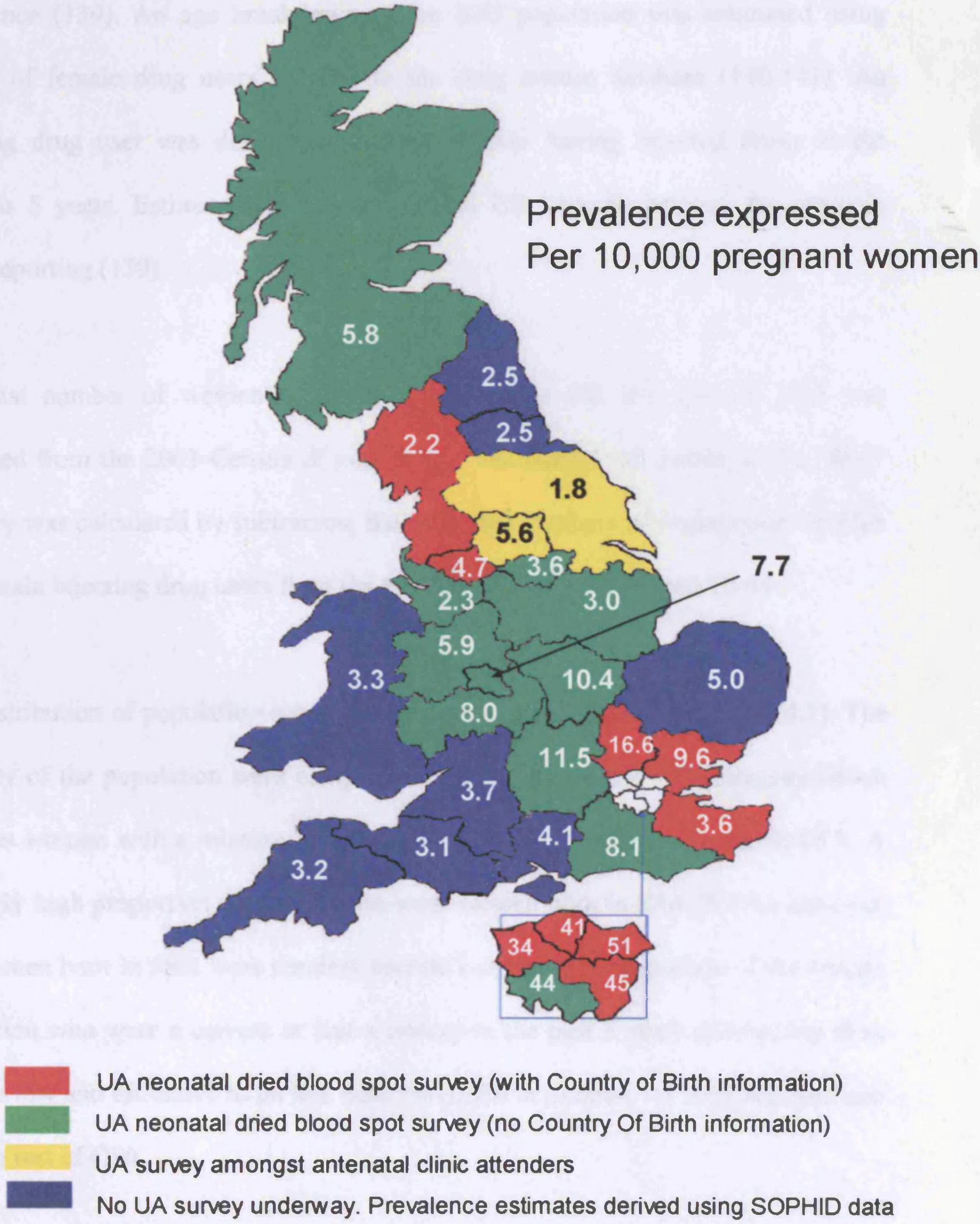
Women born in SSA had the highest HIV prevalence in all areas of GB. The HIV prevalence ratio for women born in SSA versus Rest was 37 (2.50% versus 0.068%) in London, 44 (1.98% versus 0.045%) in Scotland and 140 (2.25% versus 0.016%) in the rest of GB. HIV risk amongst drug users was substantially lower than women born in SSA, although higher than amongst other women. For IDUs the prevalence ratio versus rest was 4 (0.29% versus 0.068%) in London, 10 (0.43% versus 0.045%) in Scotland and 27 (0.43% versus 0.016%) in the rest of GB (Table 4.1).

Table 4.1: Estimates of the HIV risk, population size and numbers of live births by population sub group: 2002

	London	Scotland	Rest (
HIV prevalence in pregnant women in 2002[1]	0.38%	0.058%	0.050
	(422/105,817)	(30/51,288)	(234/469
Prevalence in women born SSA[2]	2.50%	1.98%	2.25
(prev. ratio women born in SSA vs rest)[3]	(37)	(44)	(140
Prevalence in Injecting drug users[2]	0.29%	0.43%	0.43
(prevalence ratio IDU vs rest)[3]	(4)	(10)	(27)
Prevalence in Rest	0.068%	0.045%	0.016
Number of live births in 2002[4]	103,135	52,527	485,4
% born SSA	13.04%	0.52%	1.37
% Rest (including IDUs)	86.96%	99.48%	98.63
Population size (females aged 16-44 years)[5]	1,737,820	1,062,239	8,778,
% born SSA	9.2%	0.6%	1.3
% IDU	0.5%	0.9%	0.3
% Rest	90.3%	98.5%	98.4

[1] Data analysed from the unlinked anonymous neonatal seroprevalence survey
[2] Using reports of HIV infected women made to the National Study of HIV in Pregnancy and Childhood it was estimated that in London 84% of infection was in women born in SSA, 1% of infection was in IDUs and 15% of infection was in Rest. In Scotland 18% of infection was in women born in SSA, 5% of infection was in IDUs and 77% of infection was in Rest. In rest of GB 64% of infection was in women born in SSA, 4% of infection was in IDUs and 32% of infection was in Rest. These estimates combined with numbers of live births were used to derive category-specific prevalences for pregnant women. For example HIV prevalence in women born in SSA and resident in Scotland was ((30*0.18)/(52527*0.0052)*100). An estimate of numbers of live births to IDUs were estimated using data from NATSAL previously analysed by Ades et al (138).
[3] The ratio by which the prevalence of infection is greater than the prevalence in 'Rest' women
[4] Unpublished data from birth registration records obtained from the ONS and GRO
[5] Unpublished data from the 2001 census of population survey obtained from the ONS and GRO

Figure 4.1: Neonatal HIV seroprevalence in 2002



4.3: Estimate of live birth rates using routine data

4.3.1: Population size

The number of female IDUs in GB was derived using published estimates of drug prevalence (139). An age breakdown of the IDU population was estimated using reports of female drug users notified to the drug misuse database (140-141). An injecting drug user was defined as current or ever having injected drugs in the previous 5 years. Estimates of drug use within GB have limitations, for example under reporting (139).

The total number of women aged 16-44 resident in GB and born in SSA was estimated from the 2001 Census of population. The number of women in the 'Rest' category was calculated by subtracting the estimated numbers of women born in SSA and female injecting drug users from the total number of women aged 16-44.

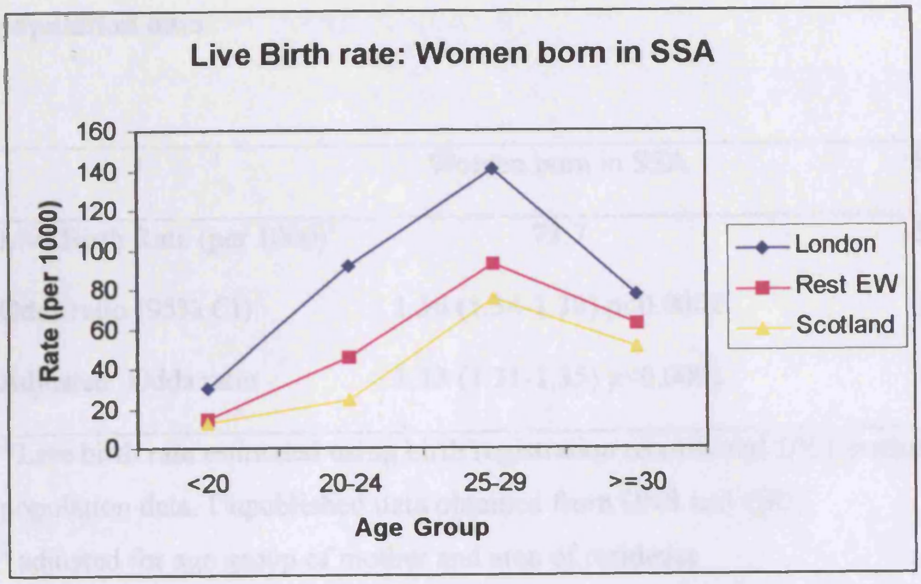
The distribution of population sub-groups varied by geographic area (Table 4.1). The majority of the population were categorised as Rest, a low risk HIV category which includes women with a mixture of ethnicities and countries of birth outside SSA. A relatively high proportion within London were women born in SSA (9.2%), although few women born in SSA were resident outside London. The proportion of the female population who were a current or had a history in the past 5 years of injecting drug use was low and estimated to be less than 1% (0.5% in London, 0.9% in Scotland and 0.3% in rest of GB).

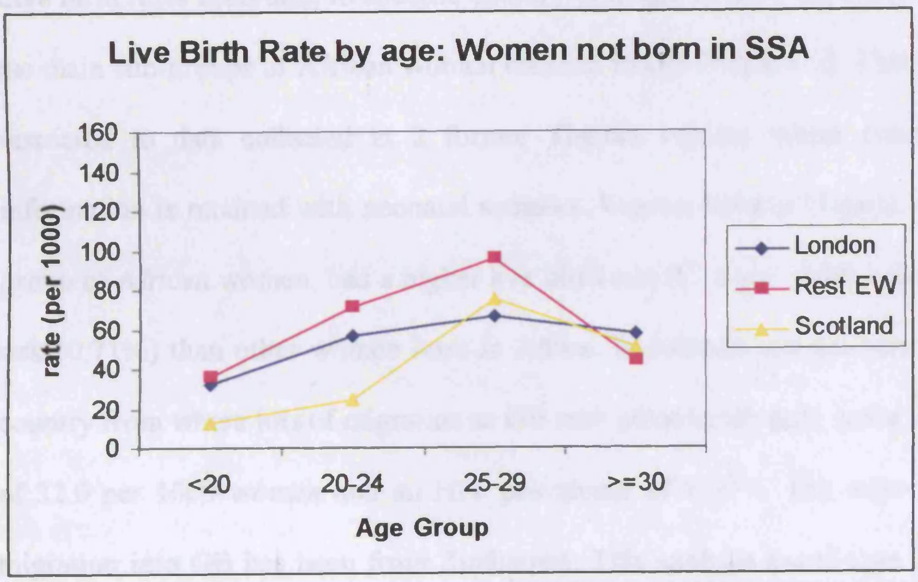
4.3.2: Live births

Numbers of Live births for women born in SSA and 'Rest' in 2002 were estimated using birth registration records which include information on country of birth (unpublished data obtained from ONS (E&W) and GRO (Scotland)). Routinely available fertility information amongst IDUs was limited and was not estimated in this particular analysis. Live birth rates (number of live births divided by population size) were estimated and expressed as rates per 1000 women. Logistic regression analysis was used to obtain odds ratios (OR) and 95% Confidence Intervals (CI) using STATA 8.2 (142).

Live birth rates varied by country of birth, age group and area of residence. Women born in SSA and resident in London had higher fertility rates than other women and the peak age group of fertility for all women was 25-29 years (Figure 4.2). The live birth rates for women born in SSA and Rest were 73.7 and 55.1 per 1000 women respectively (Table 4.2). Adjusting for age and area, women born in SSA were 1.3 times more likely to have a live birth than Rest (OR 1.33, CI (1.31,1.35), $p<0.0001$) (Table 4.2).

Figure 4.2: Live birth rate[1] by age: Great Britain





[1] Live birth rate estimated using birth registration records and 2001 census of population data. Unpublished data obtained from ONS and GRO.

Table 4.2: Adjusted Odds Ratios for Live births in women in Great Britain using population data

	Women born in SSA	Rest
Live Birth Rate (per 1000)[1]	73.7	55.1
Odds ratio (95% CI)	1.36 (1.34-1.38) p<0.0001	1.00
Adjusted[2] Odds ratio	1.33 (1.31-1.35) p<0.0001	1.00

[1] Live birth rate estimated using birth registration records and 2001 census of population data. Unpublished data obtained from ONS and GRO.

[2] adjusted for age group of mother and area of residence

Live birth rates according to specific country of origin in SSA were also analysed for the main sub-groups of African women resident in GB (Table 4.3). This analysis was restricted to data collected in 2 former Thames regions where country of birth information is retained with neonatal samples. Women born in Nigeria, GB's largest group of African women, had a higher live birth rate (87.6 per 1000) and a lower HIV risk (0.71%) than other women born in Africa. In contrast women born in Kenya, a country from where lots of migration to GB took place in the past, had a live birth rate of 32.0 per 1000 women and an HIV prevalence of 1.69%. The majority of recent migration into GB has been from Zimbabwe. This analysis found than Zimbabwean women resident in GB had both a high live birth rate (77.8 per 1000) and a high HIV risk (10.26%) compared to other women originating from Africa.

Table 4.3: HIV Prevalence and Live Births amongst women in Thames[1] by Country of birth within Africa in 2002

	HIV Prevalence (%)[2] (No. Positive/No. Tested)	Population size[3]	Live birth rate (per 1000)[4]
Nigeria	0.71 (13/1839)	25,287	87.6
Kenya	1.69 (13/771)	24,494	32.0
South Africa	1.32 (9/684)	17,078	49.8
Zimbabwe	10.26 (47/458)	7211	77.8
Other	2.38 (151/6336)	83,093	119.8
Total	**2.31 (233/10088)**	**157,163**	**91.4**

[1]Data for the former North Thames and South East Thames Regions

[2] Estimates derived from unlinked anonymous testing of pregnant women

[3] Estimates derived from 2001 census of population data (unpublished data)

[4] Live birth rate estimated using birth registration records and 2001 census of population data. Unpublished data obtained from ONS and GRO.

In summary, women born in SSA experienced both higher live birth rates and HIV risk than the rest of the population, and HIV prevalence and fertility varied substantially depending on which country of Africa the woman had been born in. The following numerical example shows the effect of differential fertility amongst Africans on HIV prevalence estimates using data presented in Table 4.1. Within London, an area with substantial adult populations from Africa, application of a dried blood spot prevalence (0.38%) to a population unadjusted for country of birth (1,737,820) would overestimate the total number of infections amongst women by approximately 30% (6600 unadjusted compared with 5100). Outside London numbers of infections would be overestimated by approximately 10% (4400 unadjusted compared with 4050 adjusted). This analysis highlights the importance of ongoing monitoring of differential fertility and HIV patterns amongst women born in SSA when interpreting neonatal seroprevalence data as changes in these patterns will be reflected in trends of HIV prevalence.

4.4: Fertility in women who first tested HIV-positive during pregnancy

As we were unable to obtain reliable estimates of numbers of live births to IDUs, results from the previous analysis were supplemented with fertility information (previous live births, terminations, miscarriages and stillbirths) collected as part of a European cohort study of diagnosed HIV-infected pregnant women which includes 4 centres in GB (35). This supplementary analysis was restricted to fertility prior to HIV diagnosis as knowledge of HIV status may influence future fertility decisions. Fertility amongst IDUs was analysed separately for current and past injectors and this was based on the assumption that patterns may vary amongst the two groups of drug users. A current injecting drug user was defined as having injected drugs during pregnancy and/or evidence of drug withdrawal symptoms in the neonate. A past IDU was defined as having injected drugs prior to, but not during, pregnancy. Univariate and multivariate logistic regression was used to obtain ORs and 95% CI, using STATA version 8.2 (142).

By May 2004 4541 HIV-infected women had enrolled in the ECS. The number of patients recruited from each country ranged from 20 in Denmark to 1363 in Italy. One hundred and fifteen women were enrolled from GB, the majority of which were from Edinburgh. Analyses were restricted to previous live births in 1698 women who had been pregnant before the time of their first HIV test. Twenty three percent (393/1698) were born in SSA, 18% (314/1698) of the women were current IDUs, 20% (341/1698) were past IDUs and 33% (560/1698) were women in the Rest category. In 90 (5%) cases there was insufficient demographic information to assign a risk category. Women in Spain, Poland and Italy were more likely to have a history of drug use than women in the other countries. Few (5) women born in SSA had a history of drug use.

A woman's fertility was associated with the population subgroup she belonged to; 53% (203/383) of women born in SSA had had at least 1 previous live birth compared to 37% (108/292) for current IDUs, 28% (90/320) for past IDUs and 35% (187/537) for Rest (Table 4.4). Adjusting for age at HIV diagnosis, women born in SSA were 1.99 (CI (1.51-2.63), $p<0.001$) times more likely to have had a previous live birth than women categorised as Rest. Current IDUs also had a higher likelihood of having had a previous livebirth, although this was not significant (OR 1.15, CI(0.85-1.55), $p=0.38$). Past IDUs were less likely to have had a previous live birth (OR 0.69, CI(0.51-0.95), $p=0.02$).

Current and past IDUs were more likely to have had a termination than women categorised as rest (OR 1.48 and 1.51 respectively). Women born in SSA were also more likely to have had a previous termination, although this was not statistically significant (Table 4.4). Previous studies have also observed black women were more likely to have had an abortion than other women (143-144). No differences between the sub-groups of women were found in the likelihood of having a previous miscarriage or stillbirth (data not shown).

The biases associated with differential fertility in IDUs in relation to the interpretation of neonatal seroprevalence data have not been considered prior to this analysis. Results showed that IDUs were less likely to have had a previous live birth than other women, and more likely to have had a previous termination. Previously published literature in this area, though limited, is consistent with these results (68,145-146). Whilst uncertainty remains in the fertility of IDUs in GB, these analyses highlight that drug users constitute a relatively small proportion of the British population and their HIV risk in women who become pregnant is low. Any biases associated with this group in estimating population prevalence will therefore be limited. Based on results from these analyses, IDUs will not be included in the final adjustment model as a separate sub-group of women.

Table 4.4: Pregnancies in women who first tested HIV positive during pregnancy (ECS)[1]

	SS Africa (n=393)	Current IDU (n=314)	Past IDU (n=341)	Rest (n=560)
Numbers of previous live births				
0	180 (47%)	184 (63%)	230 (72%)	350 (65%)
1 or more	203 (53%)	108 (37%)	90 (28%)	187 (35%)
Not Known[3]	10	22	21	23
Odds Ratio (95% CI)	2.11 (1.61-2.76) $p<0.001$	1.09 (0.82-1.48) $p=0.53$	0.73 (0.54-0.99 $p=0.004$	1.00
Adjusted[2] Odds Ratio (95% CI)	1.99 (1.51-2.63) $p<0.001$	1.15 (0.85-1.55) $p=0.38$	0.69 (0.51-1.95) $p=0.02$	1.00
Numbers of previous Terminations				
0	271 (73%)	199 (69%)	215 (68%)	402 (76%)
1 or more	102 (27%)	91 (31%)	101 (32%)	124 (24%)
Not Known[3]	20	24	25	34
Odds Ratio (95% CI)	1.22 (0.90-1.65) $p=0.19$	1.48 (1.07-2.04) $p=0.02$	1.52 (1.12-2.08) $p=0.01$	1.00
Adjusted[2] Odds Ratio (95% CI)	1.20 (0.89-1.63) $p=0.23$	1.48 (1.08-2.05) $p=0.02$	1.51 (1.10-2.06) $p=0.01$	1.00

[1] The European Collaborative Study includes 20 centres from 10 countries in Western Europe, including GB

[2] adjusted for age group of mother at time of HIV diagnosis

[3] Cases not known were not included in the analysis

4.5: Fertility in women participating in a behavioural study in GB

The National Study of Sexual Attitudes and Lifestyle (NATSAL) is a population survey carried out to provide an insight into behavioural patterns in GB. In addition to the main study, a focussed study among Britain's ethnic minorities was undertaken to enable reliable analyses across ethnic groups. Data from NATSAL are commonly presented as weighted values to adjust for the unequal probability of selection (137). Firstly, the demographic characteristics of African women compared to other women was assessed using descriptive statistics. Finally, the likelihood of having had a previous livebirth and the factors associated with this were analysed using a logistic regression analysis.

Table 4.5 shows the demographic composition of the women participating in NATSAL. As expected, since NATSAL is a random sample, most women (86.7%) lived outside of London. Most of the women in the study were white (91.7%), 2.9% were south Asian, 1.1% were black African and 2.0% were black Caribbean. The equivalent figures in the 2001 census were 91.9% white, 3.6% south Asian, 0.8% black African, 0.9% black Caribbean and 2.8% Other. Differences reflect the ethnic boosting of the NATSAL sample. The greatest proportion (62.9%) of women were either married or co-habiting and only 7.6% were divorced, separated or widowed (Table 4.5). Compared to other women, black Africans were more likely to live in London, be older and be more likely to be divorced/separated or widowed than other women (data not shown).

Among women in NATSAL, 28.6% (1986 of 6942) had had a birth in the last 5 years. The proportion of women with a live birth was highest in black African women

(45.0%), among women aged 25-34 years (41.0%) and amongst women who were married (39.9%) (Table 4.6). Among women who had a child, 54.5% were married, compared to 16.0% among women without a child (Data not shown). Compared to other women, African women were less likely to have no children (30.8% compared to 40.3%), more likely to have 3+ children (32.3% compared to 16.3%), more likely to have had a miscarriage (31.7% compared to 20.7%) and more likely to have had a termination of pregnancy (38.5% compared to 16.6%) (data not shown).

Logistic regression confirmed that fertility was significantly associated with age, ethnicity and marital status after adjusting for age, ethnicity, marital status and residence (Table 4.6). Black African women were over twice as likely to have had a livebirth in the past 5 years than other women (OR 2.85, 95% CI 2.14-3.80, $p<0.001$), confirming our previous analyses in this chapter. South Asian women had significantly higher fertility than White women, although this was not significant after adjustment for age, partnership status and residence. Women who were single were nearly 5 times less likely to have had a livebirth in the previous 5 years than married women (OR 0.18, 95% CI 0.15-0.21, $p<0.001$).

Table 4.5: Demographic profile of women in NATSAL*

Demographics		**Total (%)**
Residence	London	13.3%
	Rest GB	86.7%
Age group	16-24	25.7%
	25-34	37.6%
	35-44	36.8%
Partnership status	Married	44.6%
	Div/sep.	7.3%
	Widowed	0.3%
	Single	29.5%
	Co-habiting	18.3%
Ethnicity	White	91.7%
	S. Asian	2.9%
	Black African	1.1%
	Black Caribbean	2.0%
	Other	2.4%
Weighted, unweighted base		**5785, 6942**

*Analysis of NATSAL restricted to women aged 16-44 years. All percentages are of column weighted base.

Table 4.6: Odds ratio of having had a live birth in the previous 5 years (NATSAL)

	Total (n)	Birth last 5 years N (% of n)	Crude OR	P value	Adjusted OR	P value
Total (Unweighted)*	6942	1986 (28.6%)	-		-	
Ethnicity						
White	5697	1537 (26.9%)	1.0		1.0	
Black African	271	122 (45.0%)	2.22(1.73-2.85)	<0.001	2.85(2.14-3.80)	<0.001
Black Caribbean	354	110 (31.1%)	1.22(0.97-1.54)	0.094	2.10(1.62-2.72)	<0.001
South Asian	410	149 (36.3%)	1.55(1.26-1.91)	<0.001	1.26(0.99-1.58)	0.051
Other	186	65 (34.9%)	1.46(1.07-1.98)	0.017	1.45(1.03-2.04)	0.033
Residence						
London	5112	1438 (28.1%)	1.0		1.0	
Outside London	1830	548 (29.9%)	1.09(0.97-1.23)	0.140	0.96(0.83-1.10)	0.539
Age group						
16-24	1567	334 (21.3%)	1.0		1.0	
25-34	2748	1127 (41.0%)	2.57(2.23-2.96)	<0.001	1.30(1.10-1.53)	0.002
35-44	2627	525 (19.9%)	0.92(0.79-1.08)	0.302	0.35(0.28-0.42)	<0.001
Partnership						
Married	2721	1087 (39.9%)	1.0		1.0	
Co-habiting	1038	332 (31.9%)	0.71(0.61-0.82)	<0.001	0.52(0.44-0.61)	<0.001
Div./Sep./Wid.	783	184 (23.5%)	0.46(0.38-0.55)	<0.001	0.43(0.36-0.52)	<0.001
Single	2383	380 (15.9%)	0.29(0.25-0.33)	<0.001	0.18(0.15-0.21)	<0.001

*Data presented as unweighted values in order to maximise sample size

4.6: Key points

1. This analysis has quantified the fertility differentials in the main population sub-groups at varying risk of HIV infection in GB using a number of different data sources. It has identified data sources available for inclusion in an adjustment model to improve the interpretation of neonatal data for differential patterns of HIV and fertility amongst women in GB.

2. Women born in SSA experienced both higher live birth rates (73.7 versus 55.1 per 1000) and HIV risk (2.5% versus 0.38%) than the rest of the population and HIV prevalence and fertility varied substantially depending on which country within Africa the woman had been born in, area of residence within GB and age group. These results suggest that without adjusting for country of birth, previous estimates of HIV in the general heterosexual population may have been biased upwards.

3. The biases associated with differential fertility in IDUs have not previously been considered. Results showed that IDUs were less likely to have had a previous live birth than other women (OR 0.69) and more likely to have had a previous termination (OR 1.51), a finding consistent with previously published literature. This analysis highlighted that drug users constitute a relatively small proportion of the British population (<1%) and their HIV risk in women who become pregnant is low (0.29% in London). Any biases associated with this group in estimating general population prevalence will therefore be limited.

4. Within Britain the size of population sub-groups born abroad and HIV risk of different groups is a changing dynamic. The ongoing monitoring of fertility and HIV risk amongst women born abroad will be important and if any changes occur, the adjustment model will need to be adapted accordingly.

Chapter 5: Characteristics of diagnosed HIV infected women in GB: Review of routine datasets

5.1: Introduction

This chapter presents analyses undertaken to assess current fertility patterns in diagnosed HIV-infected women. As presented in more detail in the methods chapter, the data sources for this chapter are numbers of prevalent HIV infections received through the Survey Of Prevalent HIV Infections Diagnosed (SOPHID), reports of newly diagnosed HIV infections and reports of HIV-infected pregnant women received through the National Study of HIV in Pregnancy and Childhood (NSHPC). Where appropriate the outcomes of these analyses were included in the final adjustment model in chapter 7 to improve the interpretation of neonatal seroprevalence data. With the exception of SOPHID which only collects information on ethnic origin, analyses have been stratified according to whether or not the woman was born in SSA to ensure results are consistent for use with the neonatal seroprevalence data. Within the UK the majority of HIV-positive women were born in SSA, with few non-Africans born in SSA (2%) and few HIV-positive black Africans (6%) born outside SSA (unpublished data, CDSC).

5.2: Profile of HIV-infected women receiving care

The demographic profile of HIV-infected women currently receiving care in England, Wales and Northern Ireland (E,W & NI) was analysed using SOPHID data relating to women currently accessing health care in order to provide an insight in fertility patterns one may expect from such a group of women (130). A requested set of aggregate tables was obtained from CDSC and the age, risk group and clinical stage of illness was explored using 2002 data, as well as changes in characteristics of prevalent diagnosed infections since 1997. Rates of diagnosed HIV infection among women aged 15-54 years were estimated based on population data for England and Wales from 2001 census information (Unpublished data, census 2001). The census has previously been described in chapter 3. An analysis of under-reporting and non-attendance of SOPHID data to provide a more accurate assessment of caseload has been undertaken, and is estimated to be 13.5% (134,147). SOPHID data were therefore adjusted by this factor when used in the final model in chapter 7.

In 2002 30,281 individuals, including children, were seen for care in E, W & NI, of whom 30% (8967) were women (Table 5.1). Between 1997 and 2002 the number of women with HIV increased 3.2 fold (2776 to 8967) whilst over the same period the number of men with HIV increased 1.9 fold (11,460 to 21,314). Explanations for this rise in prevalence amongst women include improvements in diagnosing new infections during routine antenatal screening, reduction in HIV-related deaths due to advancements in antiretroviral therapies and the movement of HIV-infected people from countries with a high HIV prevalence to the UK.

Two thirds (64%) of women were aged between 25-39 years, the peak age group for fertility, although the proportion of women aged 40 and over has risen over time from 16% (429/2776) in 1997 to 23% (2038/8967) in 2002. The rate of diagnosed HIV infection among women aged 15-54 years in 2002 was 6.3 per 10,000 and this varied according to ethnic group; 374.2 per 10,000 for black Africans, 15.6 per 10,000 for black Caribbean's, 1.3 per 10,000 for Whites and 1.6 per 10,000 for south Asians (Indian, Pakistani and Bangladeshi) (Table 5.1). Since 1997 there has been more than a 4.4 rise in the number of women of black African (1416 to 6205) and a 3.8 fold rise in women of black Caribbean (79 to 297) ethnicity seen for HIV-related care. During the same time period there was a 2.3 fold increase and 1.7 fold increase in the number of women of south Asian and White ethnic group respectively. The rise in number of HIV-positive African women is attributed to recent immigration from countries of high HIV prevalence to the UK. The increased HIV prevalence amongst black Caribbean's is also unsurprising given that HIV is well established in the Caribbean, continuing inward migration to GB is occurring from that area, and a high incidence of bacterial STIs among Britain's black Caribbean community has been reported (148,149).

Whilst the majority of adult women with diagnosed HIV infection were resident in London (59%), the proportion of diagnosed women resident outside London has increased from 31% in 1997 to 41% in 2002 (Table 5.1). This is partly explained by the dispersal of new migrants, including asylum seekers, to different parts of the country. The prevalence of diagnosed HIV infection amongst women in London was 23.5 per 10,000 population aged 15-54 years, and in 2002 76% of those HIV-infected women resident in London were of black African ethnicity. Outside of London the prevalence of HIV diagnosed amongst adult women per 10,000 population was 2.9, and 62% of these were of black African ethnicity. The majority of women probably acquired their infection through heterosexual contact (88%), whilst few cases were attributed to injecting drug use (3%) or mother to child transmission (6%) (Table 5.1).

It has been suggested that improvements in HIV-related therapies have made many women feel better, which may in turn positively influence reproductive decision-making, the topic of interest in this thesis. Clinical stage of illness was reported for

8640 women in 2002, of whom 45% were asymptomatic. Thirty one percent had HIV-related symptoms but not AIDS and 22% had an AIDS diagnosis. For women for whom therapy was reported in 2002 (95%), 63% were on therapy of whom 96% were on triple or more drugs (Table 5.1). In contrast in 1997, 39% of women were asymptomatic, 55% were on some sort of therapy, and of those on therapy 61% were taking 3 or more drugs (Table 5.1). No differences were observed in the clinical stage of illness and level of therapy between African and Non-African women.

Table 5.1: Characteristics of diagnosed prevalent HIV infections amongst women and % change between 1997 and 2002: England, Wales and Northern Ireland

	1997	2002	% Proportion of all cases (2002)	Rate per 10,000 population*	Fold change between 1997-2002
No. of women	2776	8967	-	6.3	3.2
Age Group					
0-14	161	475	5%	0.9	3.0
15-24	177	713	8%	2.3	4.0
25-39	2009	5735	64%	9.8	2.9
40-54	370	1800	20%	3.4	4.9
55+	59	238	3%	-	4.0
Not Known	0	6	-	-	-
Ethnicity					
Black African	1416	6205	69%	374.2	4.4
Black Caribbean	79	297	3%	15.6	3.8
White	959	1663	19%	1.3	1.7
South Asian	44	103	1%	1.6	2.3
Other/NK	278	699	8%	-	-
Area of residence					
London	1864	5175	59%	23.5	2.8
Rest EW&NI	850	3605	41%	2.9	4.2
Other/Abroad	8	12	<1%	-	1.5
Not Known	54	175	-	-	-
Exposure					
Heterosexual	2214	7920	88%	-	3.6
Injecting drug use	292	292	3%	-	-
Mother to Child	158	496	6%	-	3.1
Other/NK	112	259	3%	-	-
Stage of illness					
Asymptomatic	1034	3883	45%	-	3.8
Symptoms pre-AIDS	896	2666	31%	-	3.0
AIDS	635	1902	22%	-	3.0
Other	114	189	2%	-	1.7
Not Known	97	327	-	-	-
HIV Therapy					
None	910	3161	37%	-	3.5
1-2 drugs	436	207	2%	-	0.5
3+ drugs	682	5143	61%	-	7.5
Not Known	748	456	-	-	-

*Per 15-54 women.

5.3: Newly diagnosed HIV infections amongst women

Another source of information on women with diagnosed HIV is available from infection reports (18-19). This analysis focused on age, reason for HIV test and number of previous live births in women newly diagnosed with HIV infection in GB, with results providing a useful input in the modelling of reproductive decisions. Reports of newly diagnosed infections were analysed using a dataset obtained from CDSC which contained the variables of interest for this project (Age, reason for test, ethnic group, country of birth, year of arrival in UK, probable route of exposure, date of positive test, previous live births and whether or not the woman had been pregnant at diagnosis). Fertility information has been included on the new HIV infection reports since 2000 on my request for this project and justification for this was submitted and approved by the project review team at CDSC in August 1999.

Data on parity, age, pregnancy at diagnosis and reason for HIV test were abstracted and analysed from 2,163 HIV reports received between January 2000 to August 2002. From these reports, information on previous live births was available on 1,646 (76%) records and whether or not the woman had been pregnant at diagnosis was available for 1,902 (88%) of records. Whilst little difference was observed in the proportion of missing information on previous live births for women born in SSA versus other women (23% versus 27%), women older than 45 were significantly more likely to have missing information than younger women (32% versus 23%). It is uncertain whether or not this would lead to an overestimate or underestimate in the number of previous live births in older women, however it is not likely to bias the final adjustment model as women older than 45 at diagnosis are assumed to no longer be of childbearing age and their parity information is not therefore included in the model.

The final analysis of this section looks at parity amongst all HIV-infected women compared with more general women surveyed through NATSAL, a survey carried out on a random sample of the population.

5.3.1: Age at diagnosis

Nearly 70% of the newly diagnosed HIV-infected women were aged 25-39 years (Table 5.2), the peak years of fertility. The mean age at diagnosis of women born in SSA and Rest was 31 (range 15-74) and 32 (range 16-78) years respectively. Routine statistics for England & Wales show that in the general population on average women of this age group (30-34) have a live birth rate of 94.9 births per 1000 women and this rate is similar to that seen in women aged 25-29 years (8). Few women (2.2%) were under 20 years and 8.9% were aged over 45 years (Table 5.2). The proportion of women aged 45 and above has not changed since the early 1990's (21). Women born in SSA were less likely to be under 20 or over 45 than other women.

Table 5.2: Age of newly diagnosed HIV-infected women

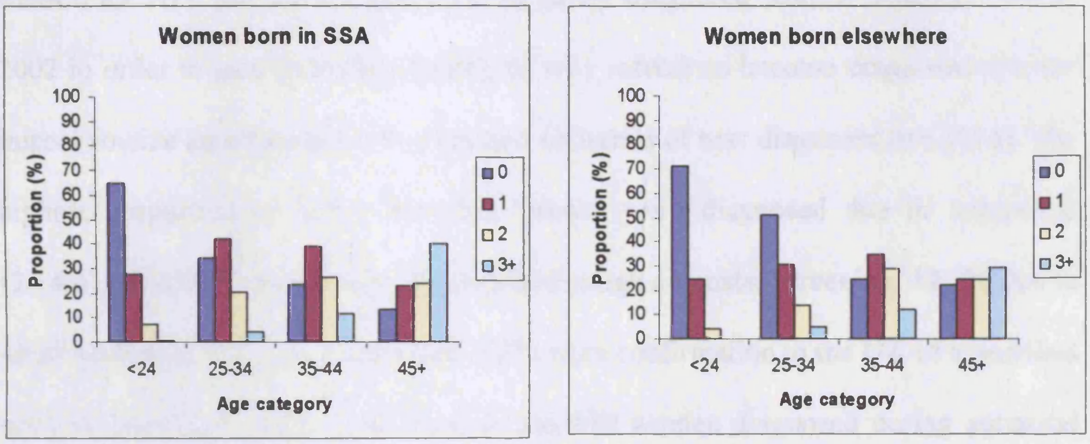
	Number of reports (%)		
	SSA	**Rest**	**Total**
15-20	24 (1.4%)	22 (5.8%)	**46 (2.2%)**
20-24	168 (9.9%)	60 (15.8%)	**228 (11.0%)**
25-29	417 (24.7%)	90 (23.7%)	**507 (24.5%)**
30-34	511 (30.2%)	71 (18.7%)	**582 (28.1%)**
35-39	298 (17.6%)	51 (13.5%)	**349 (16.9%)**
40-44	139 (8.2%)	33 (8.7%)	**172 (8.3%)**
45+	133 (7.9%)	52 (13.7%)	**185 (8.9%)**
Total	**1690 (100%)**	**379 (100%)**	**2069 (100%)**

5.3.2: Parity at diagnosis

Thirty nine percent of women born in SSA and 29% of women born elsewhere had had at least two live births at the time of their HIV diagnosis. The mean number of births was 1.4 for women born in SSA compared to 1.1 for other women. Figure 5.1

shows numbers of live births by age category. Few women aged less than 24 years old had had more than 1 child and the majority had had none. Approximately a third of women born in SSA and half of women born elsewhere who were aged 45 or under had had less than 2 children. Assuming that the average desired number of children for women born in SSA is 2.51 and other women is 2.1 (150), many of these women have yet to complete their family size at time of diagnosis.

Figure 5.1: Parity by age group and risk for newly diagnosed women



A comparison of age and parity amongst newly diagnosed HIV-infected women and all women (HIV status unknown) surveyed through NATSAL, stratified by whether or not the woman was born in SSA, suggested that birth rates before HIV diagnosis in this data set were comparable with birth rates in a more general population in NATSAL.

Over 80% of newly diagnosed women were born outside the UK, and approximately 70% of these women had arrived in the UK less than 2 years before diagnosis. This is of interest in the interpretation of neonatal seroprevalence data as previous livebirths in these women would have occurred abroad and not within the UK, thereby lessening the likelihood of these women appearing in UK neonatal seroprevalence surveys. We therefore explored country of all previous live births in newly diagnosed women to determine the likelihood of births in undiagnosed HIV-infected women being sampled in UK neonatal surveys. Of the 926/1337 women born in Africa who had had a previous live birth recorded on the report form, 92% of the live births were outside the UK.

5.3.3: Reason for HIV test

Reason for HIV test was analysed for all newly diagnosed women between 2000 to 2002 in order to gain an understanding of why infections become diagnosed and the impact routine antenatal screening has had on trends of new diagnoses (n=2,014). The highest proportion of newly reported women were diagnosed due to symptoms (36.4%), 20.4% of women were diagnosed through antenatal screening, 12.7% due to identification of HIV in a partner and 6.8% were confirmation in the UK of a previous positive test (Table 5.3). In addition to the 410 women diagnosed during antenatal care, an extra 73 women were pregnant at diagnosis, although the reason for the HIV test was HIV-related symptoms or identification of HIV in their partner. Women presenting with HIV-related symptoms were more likely to be born outside the UK than other women. Women having a confirmation of a known positive sample were most likely confirming a previous HIV diagnosis they had had outside the UK.

Table 5.3: Reason for HIV test for newly diagnosed women

Reason for HIV test	n	(%)	% born outside UK	% of those born outside UK who arrived within 2 years of diagnosis
Symptoms	733	(36.4%)	91.2%	68.7%
Known +ve partner	236	(11.7%)	82.9%	65.8%
Risky behaviour	146	(7.2%)	86.0%	73.6%
Antenatal	410	(20.4%)	89.6%	65.1%
Confirmation of known +ve	136	(6.8%)	93.2%	86.7%
Other*	71	(3.5%)	78.3%	67.5%
Not Known	282	(14.0%)	-	-
Total	**2,014**	**(100%)**	**86.2%**	**69.2%**

*includes women diagnosed through blood donation and insurance/visa screening

5.4: National Study of HIV in Pregnancy and Childhood

Characteristics of diagnosed HIV-infected pregnant women in the UK were explored using data form the National Study of HIV in Pregnancy and Childhood (NSHPC) (25). Briefly, all pregnant women known to be identified with HIV are notified through the NSHPC through a confidential reporting scheme run under the auspices of the Royal College of Obstetrics and Gynaecologists. Further details about this surveillance scheme are provided in chapter 3. A reduced dataset was obtained from the ICH containing information on demographic characteristics, year of positive test, parity, whether or not the HIV infection had been diagnosed during or before pregnancy and outcome of pregnancy. To help understand reproductive-decision making at the time of diagnosis, logistic regression analyses were performed to compare factors associated with being diagnosed during pregnancy and factors related to terminating a pregnancy after being diagnosed during antenatal care. Finally, subsequent child-bearing patterns after an HIV diagnosis were explored, in particular whether or not HIV-infected women were now more likely to want to become pregnant because of improvements in HIV management.

5.4.1: Characteristics of all reported HIV-positive pregnant women

By April 2004, 4,434 pregnancies had been reported to the NSHPC since obstetric surveillance began in 1986. Many women have had more than one pregnancy reported and the 4,434 pregnancies were in 3,626 women. The number of diagnosed pregnant women reported has increased substantially, from 86 in 1992 to 890 in 2003, a time when the general birth rate has remained stable (8). This rise was particularly apparent from 1999 onwards, when routine antenatal HIV testing was widely implemented throughout the UK (51).

Maternal characteristics are shown in Table 5.4. Eighty seven percent of women were born outside the UK, the majority of which were born in SSA. The proportion of women with a history of injecting drug use was 11% overall although this has declined significantly over the course of study, from 21% in 1990 to less than 1% in 2003 (chi-squared test for trend 55.2, $p<0.001$). HIV-infected women were shown to be having their children at an increasingly older age; average maternal age at time of HIV diagnosis increased from 21 years in 1984 to 28 years in 2004.

Table 5.4: Maternal characteristics for women reported through the NSHPC system (*N*=3626)

Maternal factor		*n*	%
Residence (*n*=3499)	London	2060	59%
	Elsewhere	1439	41%
Area of birth (*n*=2983)	SSA	2316	78%
	UK	394	13%
	Rest	273	9%
History of IDU (*n*=3344)	Yes	377	11%
	No	2967	89%
Parity (*n*=2,512)	0	976	39%
	1	879	35%
	2	402	16%
	3+	255	10%

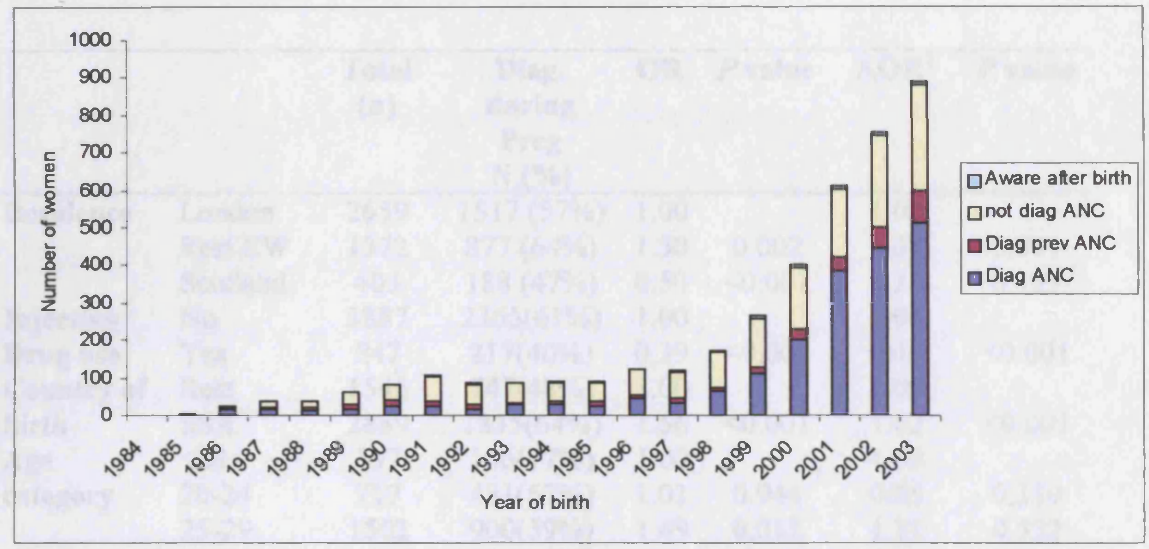
Information on previous live births was available for 69% (2512/3626) of the women, although since 1994 birth information has been missing from only 15% of reports and missing information was not associated with whether or not the woman had been born in SSA and age of the mother.

Thirty nine percent of women had had no previous children, 35% had had 1 previous child, 16% had had 2 previous children and 10% had had 3 or more. Women with a history of injecting drug use and women born in SSA were more likely to have had a previous live birth than other women (OR 1.79, 95% CI 1.11-2.86, p=0.016 and OR 1.39, 95% CI 1.14-1.69, p=0.001 respectively).

5.4.2: Timing of HIV diagnosis amongst HIV-positive pregnant women

Approximately half of the women (49%, 2188/4434) reported through the NSHPC were diagnosed during the current pregnancy, increasing from 31% (26/83) in 1990, to 42% (112/265) in 1999 to 58% (514/890) in 2003 (Figure 5.2). Two thousand one hundred and sixty (49%) of the women were aware of their HIV diagnosis prior to their pregnancy, of these a proportion (18%, 391) had been diagnosed previously in antenatal care and were going on to have a further birth. Increasing numbers of HIV-positive women know they are infected at the time they become pregnant, rising from 55 (66% of all infections) in 1990 to 145 (55%) in 1999 to 368 (41%) in 2002. A few women (2%) have been reported as having been diagnosed after the birth of their child, often because their child was unwell and was diagnosed as having HIV-related illnesses within the first 3 months of life.

Figure 5.2: Timing of maternal HIV diagnosis for women reported through the NSHPC* (*N*=4434)



*The numbers for recent years are likely to increase when late obstetric reports are incorporated and an increasing proportion of previously undiagnosed infected women have been diagnosed during pregnancy.

Table 5.5 shows the unadjusted and adjusted odds ratios for women diagnosed during pregnancy as compared to women who were aware of their infection outside of pregnancy for selected maternal characteristics. Women with a history of injecting drug use were significantly less likely to have been diagnosed during pregnancy than other women (and thus more likely to have been picked up before), and this remained significant after adjustment for residence, age and country of birth (AOR 0.44, 95% CI 0.32-0.63, $p<0.001$). In contrast women born in SSA were 1.6 times more likely to have been diagnosed during pregnancy than other women (AOR 1.62, 95% CI 1.32-1.99, $p<0.001$). Other factors significantly related to having had a diagnosis during pregnancy were residence outside London and older age (Table 5.5).

Table 5.5: OR and Adjusted OR of women diagnosed during pregnancy by demographic characteristics.

		Total (n)	Diag. during Preg N (%)	OR	*P* value	AOR[1]	*P* value
Residence	London	2659	1517 (57%)	1.00		1.00	
	Rest EW	1372	877 (64%)	1.30	0.002	1.38	0.001
	Scotland	403	188 (47%)	0.50	<0.001	1.33	0.129
Injecting Drug use	No	3887	2365(61%)	1.00		1.00	
	Yes	547	217(40%)	0.39	<0.001	0.44	<0.001
Country of birth	Rest	1545	747(48%)	1.00		1.00	
	SSA	2889	1835(64%)	1.56	<0.001	1.62	<0.001
Age category	<20	137	106(77%)	1.00		1.00	
	20-24	717	481(67%)	1.01	0.944	0.85	0.339
	25-29	1502	900(59%)	1.49	0.012	1.11	0.522
	30-34	1259	685(54%)	1.99	<0.001	1.44	0.042
	35+	649	311(48%)	2.61	<0.001	1.99	0.002

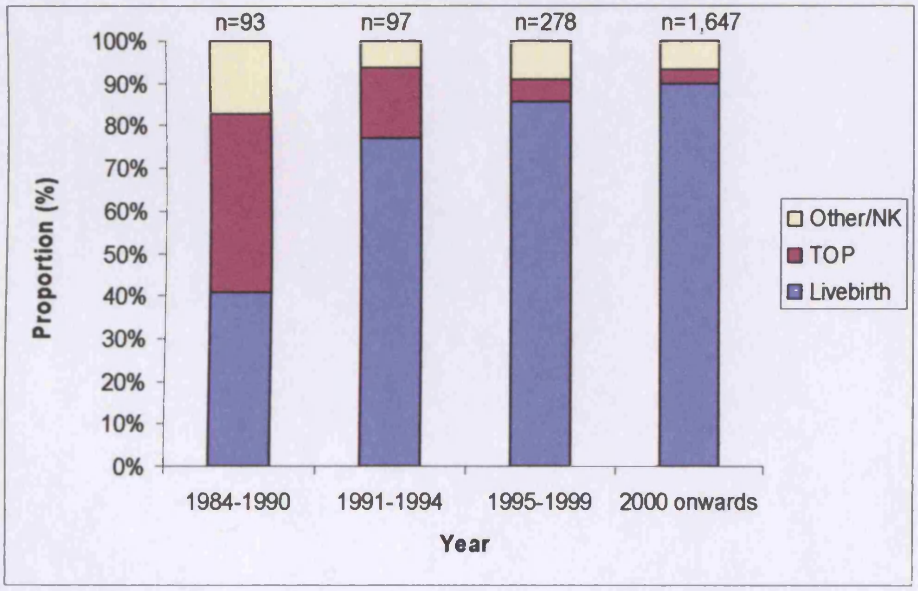
[1]Adjusted odds ratio allows for the effects of IDU, country of birth, age and residence.

5.4.3: Outcome of pregnancy in newly diagnosed HIV- positive women

The management of pregnancy in HIV-positive women has varied over time, reflecting available scientific knowledge. Some HIV-infected women opt for voluntary termination of pregnancy (TOP) and others choose to carry their pregnancy to term. Decision making is likely to be influenced by what is known about the effects of HIV on the woman and the risk of transmission to the child. This analysis looked at risk factors associated with pregnancy outcomes in newly diagnosed women to assess reproductive-decision making at time of diagnosis. Outcomes were compared prior to 1994 and 1994 onwards, as the first evidence of a sign of reduction in risk of MTCT with Zidovudine became available in early 1994. Whilst data are requested for the outcome of all pregnancies reported through the NSHPC, it is likely that notification of pregnancies not ending in a live birth is only partial but there is no reason to suggest changes over time. Odds ratios for factors related to TOP were calculated separately for each period with 95% confidence intervals. Confounding factors were analysed by logistic regression for each period.

Of the total of 2,188 women newly diagnosed during antenatal care, 1,733 (79%) proceeded to a livebirth, 128 (6%) terminated the pregnancy, 60 (3%) had a spontaneous abortion, 18 (1%) had another outcome and in 80 (3%) cases the outcome was unknown. In addition a further 169 (8%) pregnancies were continuing to term. Outcome of pregnancy has changed over time. The proportion of pregnancies ending in a termination decreased from 42% in 1984-1990 to 3.5% from 2000 onwards (Figure 5.3).

Figure 5.3: Outcome of pregnancy in women newly diagnosed during Pregnancy



After adjustment, age at diagnosis, country of birth (SSA versus Rest) and injecting drug use was not significantly associated with the decision to interrupt or continue the pregnancy during either period (Table 5.6). The following variables were significantly associated with pregnancy outcome: residence outside London since 1994 and having 1 or more child since 1994. Women resident outside London were twice as likely to have a TOP than women resident in London (AOR 2.02, 95% CI 1.11-3.67, p=0.02). This difference was not apparent pre-1994 when interventions to reduce MTCT were less available. Previous pregnancy was associated with the decision of TOP since 1994, with a higher probability of TOP among multiparas (AOR 2.27, 95% CI 1.07-4.79, p=0.03) (Table 5.6).

Table 5.6: OR and 95% CI for risk factors of TOP before and after 1994 in women newly diagnosed as HIV positive during antenatal care (n=2163*)

	Pre-1994					1994 onwards			
	Total (n)	**No. with TOP (N)**	**OR**	**AOR**	**P value**	**Total (n)**	**No. with TOP (N)**	**OR**	**AOR**
Total	263	**57**				1900	**67**		
Likely Risk of HIV(n=2163)									
Rest	37	**2**	1.0	1.0		364	**15**	1.0	1.0
IDU	124	**29**	3.43	3.98 (0.77-20.73)	0.10	26	**1**	1.40	1.78 (0.20-15.85
Born in SSA	105	**10**	1.73	1.19 (0.21-6.60)	0.84	1507	**51**	1.00	1.28 (0.57-2.84)
Residence (n=1999)									
London	105	**21**	1.0	1.0		1155	**33**	1.0	1.0
Rest EW	73	**9**	1.55	1.36 (0.49-3.76)	0.56	548	**30**	1.86	2.02 (1.11-3.67)
Scotland	85	**27**	1.92	1.21 (0.46-3.15)	0.79	33	**2**	2.05	1.18 (0.13-10.57
Age at diagnosis (n=2128)									
<20	42	**7**	1.0	1.0		94	**3**	1.0	1.0
20-24	126	**19**	0.94	1.38 (0.48-3.93)	0.55	358	**12**	1.06	0.54 (0.13-2.15)
25-29	94	**17**	1.23	2.14 (0.69-6.59)	0.18	667	**17**	0.85	0.48 (0.13-1.84)
30+	60	**3**	1.63	2.19 (0.65-7.39)	0.21	687	**26**	0.87	0.48 (0.12-1.92)
Previous live birth (n=1662)									
No	^					673	**13**	1.0	1.0
Yes	^					989	**41**	2.13	2.27 (1.07-4.79)

^ Data on parity pre-1994 not completed sufficiently enough to include in analysis

*2163 of the 2188 women who were newly diagnosed as HIV positive during antenatal care had sufficient information on year of diagnosis to be included in the analysis

5.4.4: Likelihood of subsequent live births in HIV- infected women

To inform the debate on whether diagnosed HIV-infected women are now more likely to want to become pregnant than before because of the substantial reductions in vertical transmission and the improved quality of life associated with HAART, subsequent childbearing of HIV-positive women reported through the NSHPC was analysed. All women reported through the NSHPC have had at least one pregnancy (index pregnancy). These women were categorised into 2 groups: Group 1 consisted of women who did not yet go on to have a subsequent live birth after their index pregnancy. Group 2 consisted of women who had one or more live births after their index pregnancy.

Firstly the characteristics of women with at least one subsequent live birth were compared with those without in a multivariate logistic regression analysis. Kaplan-Meier estimates of the time to subsequent live birth were obtained to find the cumulative proportion of women having a subsequent live birth according to the time period of their diagnosis (pre-1994 and 1994 onwards), and a log rank test was used to test the statistical significance of this analysis.

Sufficient data to determine subsequent live births was available for 3477/3626 (96%) of women reported through the NSHPC, of which 1292 (37%) have had a subsequent pregnancy. The main characteristics of these women are shown in Table 5.7. Women who were more likely to have a subsequent live birth in univariate analyses were more likely to have a history of injecting drug use, live in London or Scotland, be younger at diagnosis or to have already had 2 children. Women born in SSA were less likely to have had a subsequent live birth than other women. Years since diagnosis was associated with having a subsequent live birth, although only 11% of women who had had a subsequent live birth had been diagnosed in the previous 3 years. In multivariate analyses all these factors remained significantly associated with subsequent pregnancy. Women born in SSA remained less likely to have a pregnancy than other women (OR 0.73, 95%CI 0.57-0.93, $p<0.044$).

Information on subsequent live birth and timing to live birth was available for 2,875 women. A Kaplan-Meier analysis showed a significant decrease in time to subsequent live birth over time (chi square 124.87, $p<0.001$), suggesting the number of women who have subsequent live births is increasing over the years (Figure 5.4). Women diagnosed from 1994 onwards had a significantly shorter time to livebirth than women diagnosed before 1994, with 38% having a subsequent livebirth within 5 years of the index delivery, compared to 23% for women diagnosed pre-1994.

Figure 5.4: Kaplan Meier analysis of time to subsequent pregnancy, by time period

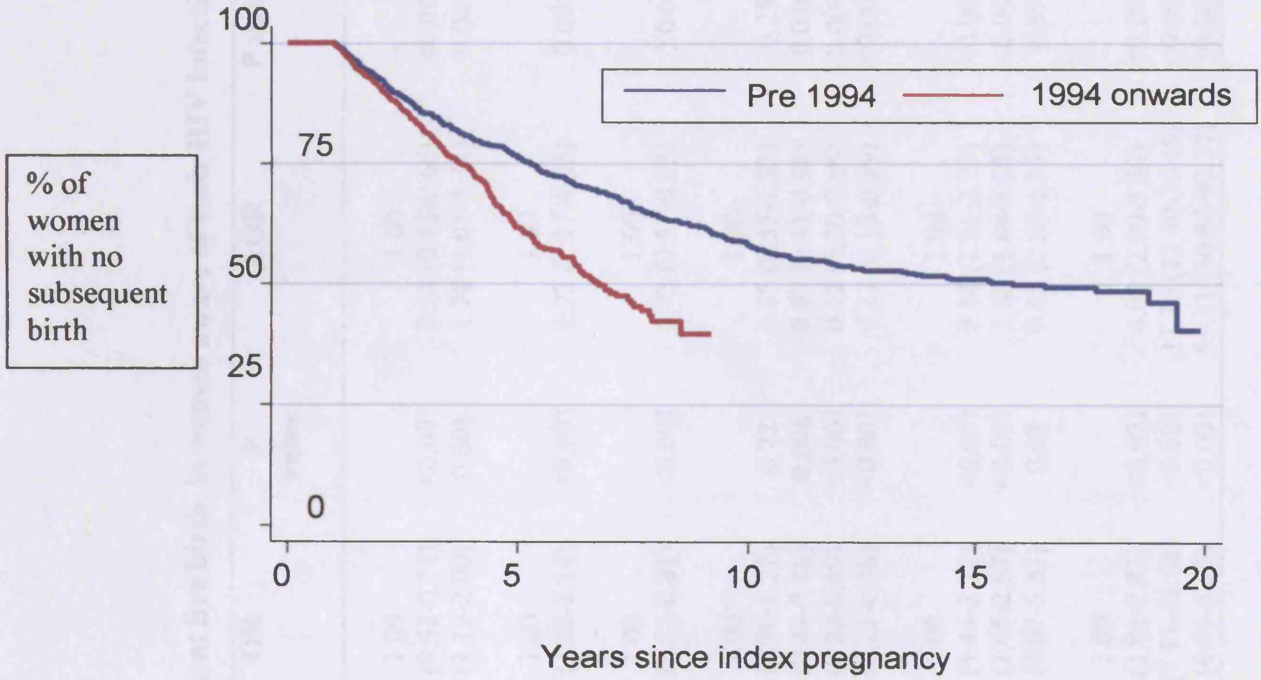


Table 5.7: OR and 95% CI for risk factors related to having had a subsequent live birth in women aware of their HIV infection

		Total (n=3477)	Subsequent pregnancy (*n*=1292)	OR	P value	AOR	P value
Residence (n=3189)	London	2055	811 (39%)	1.00		1.00	
	Rest EW	877	253 (29%)	0.62 (0.52-0.74)	<0.001	0.52 (0.41-0.66)	<0.001
	Scotland	257	129 (50%)	1.54 (1.19-2.00)	0.001	1.78 (1.01-3.14)	0.045
Injecting drug use (n=3370)	No	2993	1038 (35%)	1.00		1.00	
	Yes	377	209 (55%)	1.65 (1.28-2.14)	<0.001	2.22 (1.17-4.25)	0.001
Country of birth (n=3477)	Rest	1172	515 (44%)	1.00		1.00	
	SSA	2305	777 (34%)	0.68 (0.57-0.81)	<0.001	0.73 (0.57-0.93)	0.044
Age at diagnosis (n=3045)	<20	225	104 (46%)	1.00		1.00	
	20-24	800	359 (45%)	0.95 (0.70-1.27)	0.72	0.85 (0.55-1.33)	0.25
	25-29	1062	386 (36%)	0.66 (0.49-0.88)	0.006	0.63 (0.41-0.98)	0.036
	30-34	687	211 (31%)	0.51 (0.38-0.69)	<0.001	0.42 (0.26-0.66)	0.004
	35+	271	57 (21%)	0.32 (0.21-0.48)	<0.001	0.22 (0.13-0.39)	<0.001
Parity (n=2602)	0	881	253 (29%)	1.00		1.00	
	1	947	391 (41%)	1.75 (1.44-2.12)	<0.001	2.16 (1.71-2.75)	<0.001
	2	432	198 (46%)	2.10 (1.65-2.67)	<0.001	2.48 (1.84-3.35)	<0.001
	3+	342	125 (37%)	0.62 (0.07-5.57)	0.03	0.48 (0.83-1.35)	0.89
Yrs since diagnosis (n=3477)	<3	876	140 (16%)	1.00		1.00	
	3-5	1084	326 (30%)	2.26 (1.81-2.82)	<0.001	4.02 (2.90-5.59)	<0.001
	5-10	574	364 (63%)	9.11 (7.11-11.68)	<0.001	17.70 (12.40-25.19)	<0.001
	10+	943	462 (49%)	5.05 (4.04-6.30)	<0.001	53.11 (30.64-92.77)	<0.001

5.5: Key points

1. The number of women with diagnosed HIV infection accessing health care has increased over 3-fold in the last 5 years. The majority of these women were black African, within child-bearing age, and without AIDS-related symptoms.
2. Newly diagnosed HIV reports indicate many infected women would not appear in neonatal surveys, either because they were not of childbearing age or they had already had their children at time of diagnosis; 9% of infections were amongst women aged >=45 years and 39% of women born in SSA and 29% of other women had already had 2 or more live births by the time of diagnosis and unlikely to have more. Over 90% of live births to women born abroad had been outside the UK and would not have been picked up in the British neonatal seroprevalence surveys.
3. Whilst the number of newly diagnosed HIV infections amongst women aged >=45 years has remained steady over time, the proportion of diagnosed prevalent HIV infections amongst older women has risen due to longer survival of HIV-infected patients.
4. Increasing numbers of HIV-positive women proceeding to live birth have been reported, from 86 in 1992 to 890 in 2003. Over half (58%) of women reported in 2003 had been diagnosed during the current pregnancy.
5. The proportion of pregnancies amongst women newly diagnosed during antenatal care ending in a termination has declined from 42% in 1984-1990 to 3.5% from 2000 onwards. Decision to terminate a pregnancy was related to residence in E&W outside London (AOR 2.02) and having 1 or more child (AOR 2.27).

6. Women resident in E&W outside London, older women and women born in SSA were less likely to have a pregnancy subsequent to their HIV diagnosis than other women.
7. The proportion of HIV-positive women with subsequent live births after their diagnosis has been increasing over the years.

Chapter 6: The impact of an HIV diagnosis on fertility: Main findings from a cross-sectional survey

"I certainly want more children. The problem is having the confidence of having a baby and then going through the tests after the birth. The waiting is traumatic. It is hard enough I am positive"

(African mother with 2 HIV negative children)

6.1: Introduction

This chapter describes results from a questionnaire survey carried out amongst diagnosed HIV- positive women to assess whether improvements in treatments which delay HIV disease progression and the increasing availability of effective interventions to reduce mother to child transmission (MTCT) are associated with changes in reproductive decision-making amongst women. Results from this survey are then used in chapter 7 to interpret whether changes in decision-making have been reflected in increases in neonatal HIV seroprevalence.

The chapter is divided into 2 sections. The first section summarises the demographic characteristics, clinical condition, pregnancy history and desire for children in women recruited into the questionnaire survey. As the study population consisted of a high proportion of black African women and fertility is strongly associated with ethnic grouping, the demographic profile of African women was compared to other women. The second section assesses the representativeness of HIV-positive women surveyed compared with all women receiving HIV-related care in E&W as gathered by SOPHID. In addition, a comparison is made of the pregnancy history in women recruited into the survey with all women in the general population surveyed through NATSAL. Finally the limitations of the questionnaire survey are discussed.

Section 6A: Main findings from questionnaire survey

6A.1: Introduction

The methodology of the survey was described in detail in chapter 3. In summary, the study involved HIV positive women aged 16-49 years receiving care in centres in GB selected according to their caseload of HIV-positive women. Women self-completed a questionnaire which requested details about their demographic and clinical characteristics and their fertility history. This section begins with detailing study objectives and describing data preparation and analyses. The study population characteristics are then presented followed by results from the main analyses of this survey. Additional results from analyses are presented in appendix F.

6A.2: Study Objectives

The study had three main objectives:

- To identify factors associated with desire for children.
- To investigate whether improvements in treatments which delay HIV disease progression and interventions which reduce vertical transmission have altered women's desire for children.
- To subsequently apply the results from this survey to evaluate whether HIV-positive women desire and expect fewer children than the general British population and eventually to inform the interpretation of trends in HIV prevalence in GB using neonatal samples.

6A.2.1: Data Preparation

Responses were entered onto the computer into an Access database. The distribution of each variable was checked by one-way frequency tables for categorical variables and by histograms and the calculation of summary measures (means, standard deviations, medians and ranges) for quantitative variables. Consistency checks were performed by searching for inconsistent information between variables.

6A.2.2: Variables and outcome measures

All the variables examined in section A were collected as part of the questionnaire survey. Variables were divided into four main groups (demographic, HIV history, pregnancy history and desire for children).

Five different outcomes were measured

- Desire for (more) children
- Impact of an HIV diagnosis on fertility desire
- Association of fertility desire and improvements in treatments to delay HIV disease progression
- Association of fertility desire and improvements in interventions to reduce MTCT transmission
- A pregnancy subsequent to HIV diagnosis

6A.2.3: Data analysis

Univariate analysis was performed to determine factors associated with fertility. Variables found to be significantly associated with fertility ($P<0.05$) were included in a multivariate logistic regression analysis to determine factors independently associated with childbearing. All analyses were carried out using the STATA computer program (142).

6A.3: Population studied

The study population consisted of 450 HIV-positive women (Table 6.1) which represented 39% (450 of 1160) of all women receiving HIV-related care at the participating centres during 2002. In total 20 of the 450 women participating in the survey had taken a questionnaire home for completion. In addition an extra 26 women took a questionnaire home but failed to return it. Overall, 86% (range 63-100%) of women invited to participate in the survey completed a questionnaire.

Table 6.1: Recruitment of HIV-positive women

Clinic	No. of women attending clinic*	No. of women invited to participate	No. of questionnaires completed	% response
St. Mary's	342	117	101	86%
Newham	172	116	90	78%
Chelsea & West.	277	95	79	83%
Leicester	58	51	51	100%
Manchester	68	30	19	63%
Nottingham	42	30	28	93%
Edinburgh	201	48	47	98%
Other	-	35	35	100%
Total	**1160**	**521**	**450**	**86%**

*according to SOPHID or clinic-based 2002 data

Of the 72 women who were invited to participate in the survey but did not complete a questionnaire, limited data were available on 28 (39%). These women were similar to all women in terms of age and parity and the most common reason for not completing a questionnaire was lack of interest. Of the remaining 44 women, 26 had taken the full questionnaire home for completion but had failed to return it and 18 declined interest in the project.

6A.4: Population characteristics

The demographic and main clinical details of the 450 HIV-positive women taking part in the survey are shown in Table 6.2. The majority of women were African (324/450 (72%)) and 79% of all participants were born outside the UK. Sixty three percent were resident in London, 27% in the Rest of England and 10% in Scotland. Compared to other women, African women were over 3 times more likely to live in London, reflecting the demographic patterns of settlement throughout GB (Table 6.3). The median age was 35 years (range 20-49) at the time of the questionnaire and the median time since diagnosis was 3 years (range 0-19). African women were older at diagnosis (p=0.004) and more likely to have had a recent diagnosis (p<0.001) than other women (Table 6.3). Most of the women not born in the UK came from Zimbabwe and Uganda (Figure 6.1). Many of the women (56%) born outside the UK had arrived in the country within the last 5 years, reflecting recent migration patterns between the UK and countries with high HIV prevalence.

Figure 6.1: Predominant countries of birth for women born outside UK

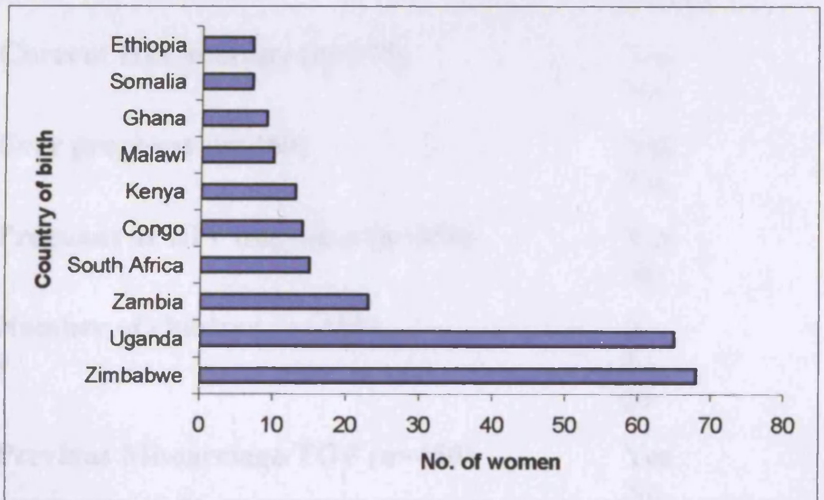


Table 6.2: Summary of demographic and main clinical details. Number (%)

	Demographic Factor	N (%)
Ethnicity (n=450)	African	324 (72%)
	Non-African	126 (28%)
Born in UK (n=450)	Yes	95 (21%)
	No	355 (79%)
Residence (n=450)	London	284 (63%)
	Rest of England	120 (27%)
	Scotland	46 (10%)
Age (n=430)	<=29	88 (20%)
	>29	342 (80%)
Years in UK (n=310)[1]	<=5 years	175 (56%)
	>5 years	135 (44%)
In a Partnership (n=450)	Yes	233 (52%)
	No	217 (48%)
Ever injected drugs (n=445)	Yes	35 (8%)
	No	410 (92%)
HIV status of partner[2] (n=233)	Positive	108 (46%)
	Negative	88 (38%)
	NK/Not tested	37 (16%)
Current HIV symptoms (n=433)	None	234 (54%)
	Mild/moderate	173 (40%)
	Severe	26 (6%)
CD4 count (n=345)	<350	194 (56%)
	>=350	151 (44%)
Current HIV therapy (n=445)	Yes	304 (68%)
	No	141 (32%)
Ever pregnant (n=450)	Yes	377 (84%)
	No	73 (16%)
Pregnant at HIV diagnosis (n=450)	Yes	130 (29%)
	No	320 (71%)
Number of children (n=450)	0	124 (28%)
	1	130 (29%)
	2+	196 (43%)
Previous Miscarriage/TOP (n=450)	Yes	181 (40%)
	No	269 (60%)
Trying for a pregnancy >6 months[3] (n=336)	Yes	73 (22%)
	No	263 (78%)

[1] For women born outside the UK. Year of arrival was not known for 45 women born outside the UK
[2] For women who had a partner [3] Only women who had wanted to become pregnant included

Overall few women had a history of injecting drug use (8%), and those that had were mainly resident in Scotland, the area of GB which experienced the most severe HIV epidemic amongst IDUs in the 1980's and early 1990's (20). Drug users were more likely to be older, of White ethnicity and to have been diagnosed with HIV infection longer than other women.

Just over half (52%) of women were in a partnership (Table 6.2): Thirty-six percent of women described themselves as either married or co-habiting, 16% had non-cohabiting partners, 27% were single and 21% were widowed, separated or divorced. Widowhood was most likely to be associated with their HIV infection. Of those women with a partner, 46% had a positive partner ("Concordant partnership"), 38% had a negative partner ("Discordant partnership") and 16% didn't know, often because the partner had not been tested. African women were more likely to be single (30% versus 21%) or widowed (10% versus 6%) than other women. Of women in a partnership, African women were also twice as likely to have a positive partner and more likely to not know their partner's status than other women (Table 6.3).

Most of the women were in relatively good health. Approximately half of the participants had no HIV-related symptoms (54%) and few (6%) had severe symptoms. Of the 77% of women who knew their current CD4 cell count, 56% had counts <350 cell/ml (Table 6.2 and Figure 6.2). Two thirds of the women were taking anti-retroviral therapy, in the majority (162, 53%) of cases 3 drugs. Disease progression and HIV symptoms were not related to ethnicity.

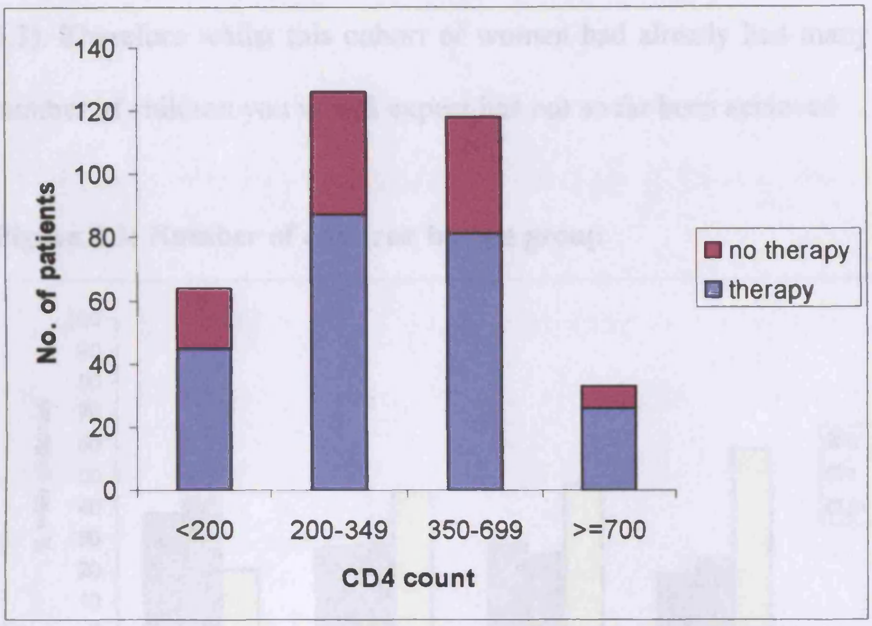
Table 6.3: Comparison of demographic profile of African women and other women

Factor[1]	Total (n)	African N (% of n)	OR	95% CI	P value
Residence (n=450)					
Non-London	166	91 (54.8%)	1.00		
London	284	233 (82.0%)	3.76	2.44-5.79	<0.001
Born in UK (n=450)					
No	355	310 (87.3%)	1.00		
Yes	95	14 (14.7%)	0.03	0.01-0.05	<0.001
In a partnership (n=450)					
No	217	166 (76.5%)	1.00		
Yes	233	158 (67.8%)	0.65	0.43-0.98	0.041
Age at diagnosis (n=450)					
<=29	211	138 (65.4%)	1.00		
>29	239	186 (77.8%)	1.85	1.22-2.82	0.004
Years since diagnosis (n=433)					
<=5 years	286	230 (80.4%)	1.00		
>5 years	147	81 (55.1%)	0.30	0.19-0.46	<0.001
History of injecting drug use (n=445)					
No	410	313 (76.3%)	1.00		
Yes	35	6 (17.1%)	0.06	0.03-0.16	<0.001
Partner HIV status (if in partnership) (n=196)[2]					
Negative	88	49 (55.7%)	1.00		
Positive	108	79 (73.1%)	2.17	1.19-3.94	0.011
No. of children pre-diagnosis (n=450)					
0	124	81 (65.3%)	1.00		
1	130	94 (72.3%)	1.39	0.81-2.36	0.230
2	114	83 (72.8%)	1.42	0.82-2.47	0.214
3+	82	66 (80.5%)	2.19	1.13-4.23	0.020
Ever had a miscarriage /TOP (n=450)					
No	269	205 (76.2%)	1.00		
Yes	181	119 (65.7%)	0.60	0.40-0.91	0.016
Trying for a preg. >6 months (n=336)					
No	263	178 (67.7%)	1.00		
Yes	73	59 (80.8%)	2.01	1.06-3.81	0.032

[1] The following variables were not significantly related to ethnicity: Age, current HIV symptoms, CD4 count, current HIV therapy, Age at first child and pregnant at HIV diagnosis

[2] Partner's HIV status NK/Not Tested in 37 cases

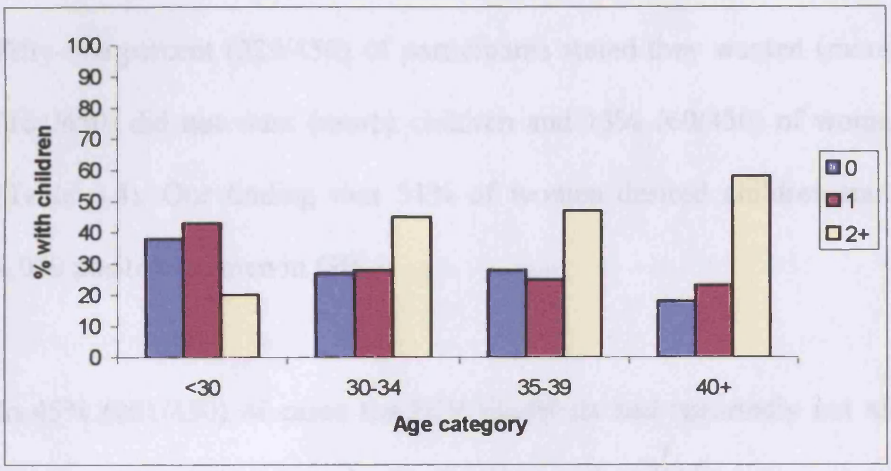
Figure 6.2: CD4 count and therapy for women in the study



The majority of the survey population had been pregnant (84%), while another 25 women (6%) were pregnant at the time of completion of the questionnaire. Many women (29%) were pregnant at the time of their HIV diagnosis, mostly as a result of the routine antenatal HIV screening programme in the UK. The mean age at first birth was 25.3 years for African women and 24.3 for non-African women. This data will be compared to all women regardless of HIV status in the next section.

The number of children a woman expects to have in her life time is associated with her ethnicity, and in general African women desire a mean number of 2.5 children whilst White women desire a mean number of 2.1 children (150). In this study 28% of women had no children, 29% had 1 child and the remaining 43% of women had 2 or more children (Table 6.2). As you would anticipate based on population statistics, African women were twice as likely to have 3 or more children than other women (Table 6.3). The number of children a woman had was also strongly associated with age and of those women aged over 40, 58% had had 2 or more children, the number of children one would expect for this age group, whilst 20% had no children (Figure 6.3). Therefore whilst this cohort of women had already had many pregnancies, the number of children you would expect has not so far been achieved.

Figure 6.3: Number of children by age group



Forty percent of women had had either a previous miscarriage or TOP. Whilst data were collected separately for miscarriage and termination, interpretation was problematic as the terms used in the questionnaire were often misunderstood by the study participants and spontaneous terminations were often confused with elected terminations. Twenty two percent (73/336) of women stated they had been trying for a pregnancy for more than 6 months; 46 (63%) of these women had sought medical help for fertility and 64 (88%) had a previous pregnancy recorded on the questionnaire. In univariate analyses, women who had been trying for a pregnancy for more than 6 months were more likely to be African (Table 6.3) and more likely to have been diagnosed with HIV for more than 5 years. No association with age was observed.

6A.5: Desire for (more) children and association of improvements in treatments and interventions

One of the main objectives of this study was to describe pregnancy decisions among HIV-positive women in light of improvements in HIV management.

Fifty-one percent (229/450) of participants stated they wanted (more) children, 36% (161/450) did not want (more) children and 13% (60/450) of women did not know (Table 6.4). Our finding that 51% of women desired children translates into over 4,000 positive women in GB.

In 45% (201/450) of cases the HIV diagnosis had reportedly not affected decision-making; 16% (72/450) had already had all the children they wanted to have, 3% (12/450) never wanted children anyway and 26% (117/450) intended to carry out their child-bearing plans regardless of their HIV infection. Of the 72 women who stated they had already had their children at diagnosis, 84% had had 2 or more children at that time. Overall 42% of women stated that their HIV diagnosis had affected their decisions; 11% (50/450) wanted children sooner whereas 31% (139/450) did not want children anymore (Table 6.4).

Factors found to be significantly associated with desire for (more) children in a multivariate analysis were partnership status, number of children the woman had already had at diagnosis and whether or not the woman had been trying for a pregnancy for more than 6 months (Table 6.5a). Women who had a partner were nearly twice as likely to desire children than other women whilst women who already had 2 or more children at diagnosis were 0.28 times as likely to desire more children.

A history of miscarriage or abortion was associated with desire for children in a univariate analysis (OR 1.55, 95% CI 1.06-2.28, p=0.024), but this did not remain significant in the multivariate model. Whilst African women were more likely to desire children than other women, this difference was also found not to be significant (AOR 1.39, 95% CI 0.77-2.49, p=0.27).

Logistic regression was also carried out to assess factors related to not wanting a child after diagnosis (155 women). Women aged older than 29 years at diagnosis and women who already had had 2 or more children were less likely to not want children whilst women who had been diagnosed for more than 5 years were more likely to not want children in univariate analyses (OR 0.53, 95% CI 0.35-0.81, p=0.003 and OR 0.46, 95% CI 0.30-0.71, p<0.001 and OR 1.74, 95% CI 1.11-2.74, p=0.016 respectively), although these associations did not remain significant in the multivariate model (Table 6.5b). African women were both more likely to desire children and to not want children after their HIV diagnosis than other women, although this was not significant in multivariate analyses. Whilst this finding may appear contradictory, African women were shown to be more likely to change their mind about desire for children since improvements in HIV management.

Table 6.4: Association of knowledge of an HIV diagnosis and improvements in treatments which delay HIV disease and interventions which reduce perinatal transmission on desire for children

Response		African women	Other women	Total
Women who want children		164 (51%)	65 (52%)	229 (51%)
	HIV diagnosis had no effect	*91 (28%)*	*26 (21%)*	*117 (26%)*
	Wanted children sooner	*32 (10%)*	*18 (14%)*	*50 (11%)*
	Didn't want children when diagnosed, although improvements in HIV management have made me desire children	*41 (13%)*	*21 (17%)*	*62 (14%)*
Women who do not want children		122 (38%)	39 (31%)	161 (36%)
	Never wanted children anyway	*6 (2%)*	*6 (5%)*	*12 (3%)*
	Already had had children at time of diagnosis	*55 (17%)*	*17 (13%)*	*72 (16%)*
	Didn't want children when diagnosed and improvements in HIV management have not made me desire children	*61 (19%)*	*16 (13%)*	*77 (17%)*
NK/Other		38 (11%)	22 (17%)	60 (13%)
Total		**324 (100%)**	**126 (100%)**	**450 (100%)**

Table 6.5a: Adjusted Odds of desiring (more) children after receiving an HIV diagnosis

	Total (n)	Desire children N (% of n)	AOR	95% CI	P value
Ethnicity					
Non-African	126	45(36%)	1.0		
African	324	140(43%)	1.39	0.77-2.49	0.27
Residence					
Non-London	166	65(39%)	1.0		
London	284	120(42%)	0.65	0.35-1.19	0.16
Years in UK					
<=5 yrs	175	75(43%)	1.0		
>5 yrs	135	63(47%)	1.41	0.77-2.59	0.27
Partnership					
No	217	71(33%)	1.0		
Yes	233	114(49%)	1.97	1.16-3.34	0.013
Age at diagnosis					
<=29 years	211	91(43%)	1.0		
>29 years	239	94(39%)	1.04	0.58-1.88	0.89
Years since diagnosis					
<=5 years	286	124(43%)	1.0		
>5 years	147	55(37%)	0.71	0.35-1.44	0.34
History of IDU					
No	410	169(41%)	1.0		
Yes	35	13(37%)	1.67	0.36-7.76	0.51
HIV-related therapy					
No	141	69(49%)	1.0		
Yes	304	115(38%)	0.88	0.50-1.55	0.66
No. of children at diagnosis					
<2	254	127(50%)	1.0		
>=2	196	58(30%)	0.28	0.15-0.51	<0.001
Ever misc/abortion					
No	269	99(37%)	1.0		
Yes	181	86(48%)	1.10	0.65-1.88	0.72
Trying for a preg >6 mo.					
No	263	92(35%)	1.0		
Yes	73	53(73%)	3.46	1.68-7.13	<0.001

Factors not found to be significant with childbearing in univariate analyses and were therefore not included in multivariate analyses were: partner's HIV status, whether the woman had been pregnant at diagnosis, current HIV symptoms, CD4 count and whether or not the woman had had a previous HIV positive child.

Table 6.5b: Adjusted Odds of not wanting a child after receiving an HIV diagnosis*

	Total (n)	Not want a child N (% of n)	AOR	95% CI	P value
Ethnicity					
Non-African	90	41(46%)	1.0		
African	266	114(43%)	2.01	0.78-5.13	0.15
Residence					
Non-London	123	57(46%)	1.0		
London	233	98(42%)	0.83	0.40-1.74	0.63
Years in UK					
<=5 yrs	182	85(47%)	1.0		
>5 yrs	138	57(41%)	1.29	0.64-2.60	0.48
Partnership					
No	178	82(46%)	1.0		
Yes	178	73(41%)	0.83	0.44-1.56	0.56
Age at diagnosis					
<=29 years	157	82(52%)	1.0		
>29 years	199	73(41%)	0.93	0.47-1.85	0.84
Years since diagnosis					
<=5 years	224	88(39%)	1.0		
>5 years	117	62(53%)	1.75	0.76-3.99	0.19
History of IDU					
No	329	140(43%)	1.0		
Yes	23	13(57%)	1.73	0.26-11.77	0.57
HIV-related therapy					
No	102	48(47%)	1.0		
Yes	249	105(42%)	0.65	0.33-1.29	0.22
No. of children at diagnosis					
<2	187	98(52%)	1.0		
>=2	169	57(34%)	1.46	0.70-3.01	0.31
Ever misc/abortion					
No	213	88(41%)	1.0		
Yes	143	67(47%)	1.11	0.59-2.09	0.75
Trying for a preg >6 mo.					
No	302	133(44%)	1.0		
Yes	54	22(41%)	0.61	0.27-1.36	0.23

*Comparison of women who did not want a child after diagnosis with women who said HIV had had no effect on their childbearing intentions

Factors not found to be significant with childbearing in univariate analyses and were therefore not included in multivariate analyses were: partner's HIV status, whether the woman had been pregnant at diagnosis, current HIV symptoms, CD4 count and whether or not the woman had had a previous HIV positive child.

The majority of women in the study were aware of the availability of treatments which delay disease progression and interventions which reduce MTCT after they had had their HIV diagnosis (95% and 91% respectively). Women who were unaware of interventions which reduce MTCT transmission were more likely to be older and to have already completed their family than other women.

The impact of improvements in treatments and interventions was analysed for the women who stated that an HIV diagnosis made them not want children any more, excluding women who stated they did not know whether they now desired children. Changes in decision-making in response to improvements in treatments and interventions to reduce MTCT was highly correlated and has therefore been presented together in Table 6.4. Forty-five percent (62/139) of women changed their minds after improvements in treatments or interventions (Table 6.4). The overall proportion of women changing their desire for children after improvements was modest (14% of the total cohort of HIV positive women).

In multivariate analysis, partnership status, taking HIV-related therapy and number of children at time of diagnosis were all strongly associated with changing desire for children since improvements in treatments which delay disease progression (Table 6.6). Women in a partnership were over 8 times more likely to change their desire for children than women without a partner, and women currently taking HIV-related therapy were 6 times more likely to change their desire than women who were not taking therapy. In contrast women with 2 or more children were over 6 times less likely to desire more children than women with less than 2 children, suggesting that women who have less than 2 children and who haven't completed their family size were now more hopeful in the light of improvements in HIV management.

The results of the multivariate analysis for the effect of increasing availability of interventions on desire for children are also shown in Table 6.6. Women who already had 2 or more children were less likely to desire children. Women who were in a partnership were over 5 times more likely to desire children than women without a partner. Women resident in London were more likely to desire children, although this did not remain significant in multivariate analyses (OR 2.24, 95% CI 1.00-4.99, p=0.048).

Table 6.6a: Adjusted Odds of wanting a child since knowledge of HIV-related treatments

	Total (n)	Wanted a child since improvements in HIV-related treatments[1]	AOR	95% CI	P value
Ethnicity					
Non-African	39	15(39%)	1.0		
African	105	34(32%)	1.25	0.19-7.85	0.81
Residence					
Non-London	51	12(24%)	1.0		
London	93	37(40%)	1.21	0.31-4.75	0.78
Years in UK					
<=5 yrs	81	28(35%)	1.0		
>5 yrs	54	18(33%)	0.90	0.26-3.10	0.87
Partnership					
No	76	16(21%)	1.0		
Yes	68	33(49%)	8.24	1.87-36.13	0.005
Age at diagnosis					
<=29 years	74	27(37%)	1.0		
>29 years	70	22(31%)	0.94	0.26-3.46	0.93
Years since diagnosis					
<=5 years	81	26(32%)	1.0		
>5 years	59	22(37%)	1.15	0.25-5.30	0.85
History of IDU					
No	129	45(35%)	1.0		
Yes	13	(3(23%)	0.27	0.01-9.54	0.47
HIV-related therapy					
No	41	12(29%)	1.0		
Yes	101	37(37%)	6.67	1.44-30.80	0.015
No. of children at diagnosis					
<2	87	35(40%)	1.0		
>=2	57	14(25%)	0.15	0.03-0.65	0.011
Ever misc/abortion					
No	80	28(35%)	1.0		
Yes	64	21(33%)	0.68	0.21-2.18	0.51
Trying for a preg >6 mo.					
No	123	39(32%)	1.0		
Yes	21	10(48%)	2.38	0.52-10.79	0.26

[1] cases consisted of women who initially did not want a child following an HIV diagnosis but then changed their minds in light of improvements in HIV management

Factors not found to be significant with childbearing in univariate analyses and were therefore not included in multivariate analyses were: partner's HIV status, whether the woman had been pregnant at diagnosis, current HIV symptoms, CD4 count and whether or not the woman had had a previous HIV positive child.

Table 6.6b: Adjusted Odds of wanting a child since knowledge of HIV-related MTCT interventions

	Total (n)	Wanted a child since improvements in interventions which reduce MTCT[1]	AOR	95% CI	P value
Ethnicity					
Non-African	38	18(47%)	1.0		
African	91	36(40%)	1.70	0.28-10.37	0.57
Residence					
Non-London	47	15(32%)	1.0		
London	82	39(48%)	1.77	0.42-7.44	0.44
Years in UK					
<=5 yrs	74	34(46%)	1.0		
>5 yrs	48	17(35%)	1.84	0.54-6.25	0.33
Partnership					
No	62	18(29%)	1.0		
Yes	67	36(54%)	5.34	1.29-22.21	0.021
Age at diagnosis					
<=29 years	68	33(49%)	1.0		
>29 years	61	21(34%)	1.20	0.33-4.38	0.78
Years since diagnosis					
<=5 years	70	27(39%)	1.0		
>5 years	56	26(46%)	1.28	0.28-5.81	0.75
History of IDU					
No	115	48(42%)	1.0		
Yes	12	5(42%)	0.49	0.01-19.63	0.70
HIV-related therapy					
No	38	17(45%)	1.0		
Yes	89	37(42%)	3.81	0.86-16.98	0.079
No. of children at diagnosis					
<2	80	41(51%)	1.0		
>=2	49	13(275)	0.15	0.03-0.64	0.010
Ever misc/abortion					
No	71	27(38%)	1.0		
Yes	58	27(47%)	1.09	0.32-3.67	0.14
Trying for a preg >6 mo.					
No	108	44(41%)	1.0		
Yes	21	10(48%)	1.25	0.26-5.90	0.78

[1] cases consisted of women who initially did not want a child following an HIV diagnosis but then changed their minds in light of improvements in HIV management

Factors not found to be significant with childbearing in univariate analyses and were therefore not included in multivariate analyses were: partner's HIV status, whether the woman had been pregnant at diagnosis, current HIV symptoms, CD4 count and whether or not the woman had had a previous HIV positive child.

6A.6: Pregnancies subsequent to HIV diagnosis

Among the 450 HIV-positive women in the study, 16% (73/450) of women had at least one pregnancy subsequent to their HIV diagnosis. Sixty one women (13%) had one pregnancy and 12 (3%) had two.

Analyses to determine factors associated with subsequent pregnancy was restricted to 312 women who had been diagnosed for at least 2 years in order to give the women a reasonable opportunity of becoming pregnant. Pregnancies varied by demographic and clinical factors: Overall women were more likely to have become pregnant subsequent to their diagnosis if they lived in London or Scotland, were 29 years or less, had been in the UK for 5 or more years, were in a partnership, had injected drugs, had no HIV-related symptoms, had been pregnant at diagnosis, had stated they wanted children sooner after their diagnosis and if they had already had one children at the time of their diagnosis (Table 6.7).

In multivariate analyses, women were most likely to have become pregnant if they were African, had been diagnosed for more than 5 years and in a partnership (Table 6.8). Women older than 29 years and women who had 2 or more children at time of diagnosis were less likely to have had a subsequent pregnancy, although this was not significant in multivariate analyses. These findings are consistent with other studies that have also shown HIV-positive black women (151) and HIV-positive younger women (100,106,151) to have more further pregnancies than other women, and with results in the general population (8).

After adjustment for all factors detailed in Table 6.8, having had a subsequent pregnancy was associated with women's desire for children at the time of their diagnosis: Women who didn't want a child were 0.29 times as likely to have had a pregnancy than women who stated HIV had had no effect (AOR 0.29, 95% CI 0.09-0.90, p=0.033). Women who wanted children sooner had more pregnancies subsequent to diagnosis than women who stated no effect, although this was not significant (AOR 1.51, 95% CI 0.43-5.28, p=0.521). It may be assumed women who change their minds about fertility due to improvements will temporarily affect trends in neonatal prevalence.. Further analyses indicated however that whilst these women had had more pregnancies than women who did not change their mind, this was not significant.

Whilst many women desired children, it was clear barriers existed against achieving this. There are many influences on an HIV-positive woman's life that may affect pregnancy decisions and a comments section within the questionnaire was used to gather further information about such factors. Key themes apparent from the comments section were that many women had no partner and a lot of those who did have a partner were in a discordant relationship. A high proportion of the women had been recently diagnosed and were still coming to terms with their condition. A disproportionately large segment of those women affected by HIV were from minority groups, often financially disadvantaged with uncertainties regarding their asylum status in the UK. Many of these women commented in the questionnaire that at present they were unable to contemplate getting pregnant. We did not specifically ask about partner's desire for children. However a previous study by Chu et al found that a similar percentage of HIV-positive men desired children as women, although the fertility desires of HIV-infected individuals did not always agree with those of their partner (151). It was not known from the questionnaire survey whether women were concerned about becoming pregnant whilst on ART. This may have contributed to the fact that only half of the women changed their mind about desire for children in light of ART. It was not known why the other half of women did not change their mind.

Table 6.7: Percentage of women pregnant since HIV diagnosis by maternal characteristic (N=312)[1]

	Demographic Factor	Pregnant after diagnosis (%)
Residence (n=312)	London	22.2%
	Rest of England	20.0%
	Scotland	30.0%
Ethnicity (n=312)	African	22.7%
	Non-African	22.9%
Age at diagnosis (n=312)	<=29	32.1%
	>29	12.7%
Years in UK[2] (n=205)	<=5 years	20.2%
	>5 years	25.9%
In a Partnership (n=312)	Yes	27.2%
	No	18.0%
Ever injected drugs (n=310)	Yes	30.3%
	No	22.0%
HIV status of partner[3] (n=144)	Positive	28.2%
	Negative	28.8%
	NK/Not tested	17.9%
Current HIV symptoms (n=303)	None	25.2%
	Mild/moderate	20.3%
	Severe	14.3%
CD4 count (n=239)	<350	20.5%
	>=350	21.4%
Pregnant at HIV diagnosis (n=312)	Yes	30.6%
	No	19.8%
Number of children pre-diagnosis (n=312)	0	18.7%
	1	35.7%
	2+	14.3%
Effect of HIV diagnosis (n=283)	No effect	22.1%
	Wanted children sooner	37.5%
	Didn't want children anymore	16.7%

[1] Analysis restricted to women who had been diagnosed for at least 2 years
[2] For women born outside the UK
[3] For women who had a partner

Table 6.8: Odds and adjusted odds of having had a pregnancy subsequent to HIV diagnosis[1]

	Total (n)	Subsequent Pregnancy N (% of n)	AOR	95% CI	P value
Ethnicity					
Non-African	105	24(23%)	1.0		
African	207	47(23%)	3.93	1.21-12.80	0.02
Residence					
Non-London	100	24(24%)	1.0		
London	212	47(22%)	1.21	0.41-3.58	0.73
Years in UK					
<=5 yrs	89	18(20%)	1.0		
>5 yrs	116	30(26%)	0.95	0.40-2.28	0.91
Partnership					
No	150	27(18%)	1.0		
Yes	162	44(27%)	2.29	1.05-5.01	0.04
Age at diagnosis					
<=29 years	162	52(32%)	1.0		
>29 years	150	19(13%)	0.54	0.23-1.28	0.16
Years since diagnosis					
<=5 years	148	18(12%)	1.0		
>5 years	147	53(36%)	4.94	1.91-12.79	0.001
History of IDU					
No	277	61(22%)	1.0		
Yes	33	10(30%)	1.55	0.25-9.67	0.64
HIV-related therapy					
No	88	23(26%)	1.0		
Yes	220	46(21%)	0.76	0.33-1.77	0.53
No. of children at diagnosis					
<2	221	58(26%)	1.0		
>=2	91	13(14%)	0.48	0.18-1.31	0.15
Ever misc/abortion					
No	180	38(21%)	1.0		
Yes	132	33(25%)	0.69	0.31-1.53	0.36
Trying for a preg >6 mo.					
No	257	57(22%)	1.0		
Yes	55	14(26%)	0.60	0.23-1.60	0.31

[1] Analysis restricted to women who had been diagnosed for at least 2 years

Factors not found to be significant with childbearing in univariate analyses and were therefore not included in multivariate analyses were: partner's HIV status, whether the woman had been pregnant at diagnosis, current HIV symptoms, CD4 count and whether or not the woman had had a previous HIV positive child.

6A.7: Summary of analyses of factors associated with fertility

The main associations of demographic and clinical factors with fertility are summarised below and in Table 6.9. Full analysis results are in appendix F. These findings are in line with previously reported findings (chapter 4 and 5) from other data sources and they therefore highlight the consistency of associations between HIV and fertility in GB.

Ethnicity

Compared to other women, African women were older at diagnosis, more likely to have had a recent diagnosis, less likely to have a partner and more likely to have 3 or more children at diagnosis. African women were also more likely to have had a further pregnancy after diagnosis. It will be important to stratify neonatal seroprevalence according to African and non-African in the final adjustment model in chapter 7.

Number of children

Women with fewer children were significantly more likely to desire more children or have changed fertility desire due to improvements in HIV-related treatments and interventions which reduce MTCT than women with 2 or more children. Therefore the number of children a woman has had at diagnosis will be an important factor to include in the adjustment model. Neonatal seroprevalence will be stratified according to whether or not the woman has had less than 2 children at time of diagnosis in the final adjustment model in chapter 7.

Partnership status

Women who were currently in a partnership (married, co-habiting or non-cohabiting partner) were more likely to desire children and have changed fertility desire due to improvements in treatments and interventions than women who were single, widowed, divorced or separated. Women who had a partner were also more likely to have had a pregnancy after their HIV diagnosis. As little data are available on partnership status of HIV-positive women, the effect of this factor will not be quantified in the final model. However, the possible influence of partnership status on the neonatal data will be discussed in chapter 8.

Age

African women were significantly older at diagnosis than other women and older women have a higher HIV prevalence than younger women. For these reasons, age will be included in the final adjustment model.

Years since diagnosis

Women who had been diagnosed for more than 5 years were more likely to have had a pregnancy after diagnosis than women who had been diagnosed 5 years or less. This relationship may reflect greater exposure to the risk of pregnancy and will not be included in the final model.

Table 6.9: Factors associated with reproductive-decision making amongst HIV-positive women: Results from univariate and multivariate analysis

Factor	Want (more) children	Pregnancy after diagnosis	Did not want a child after diagnosis	knowledge of HIV treatments	Knowledge of MTCT interventions
Demographic factors					
Ethnicity		■			
Residence					
Years in UK / Born UK					
Partnership status	■	■		■	■
History of drug use					
Clinical factors					
Age at diagnosis					
Years since diagnosis		■			
Partner's HIV status					
HIV symptoms					
CD4 count					
HIV therapy				■	
Pregnancy factors					
Number of children	■			■	■
Having had a positive child					
Previous miscarriage/TOP					
Pregnant at diagnosis					
Trying for pregnancy >6 months	■				

Significant in univariate analysis only

■ Significant in multivariate analysis

6A.8: Key points

1. In over half (56%) the cases of women an HIV diagnosis either did not affect women's desire for children or had made women want children sooner. Whilst in the remainder of cases women decided they no longer wanted children after an HIV diagnosis, nearly half of these women changed their mind once they had become aware of the advancements made in HIV management.

2. The overall proportion of women changing their fertility desire in response to knowledge of improvements in HIV management was modest (14% of the total cohort of HIV-positive women). It is unlikely therefore that changes in childbearing intentions would have greatly impacted on the doubling of neonatal seroprevalence observed between 1997 and 2002, although this will be explored in greater detail in chapter 7.

3. Number of children, partnership status and ethnicity was strongly related to women's desire for children. Women with more than 1 child were 0.28 times as likely to not want children and 0.15 times as likely to change their mind because of improvements in HIV management. African women were 3.93 times more likely to have had a pregnancy subsequent to HIV diagnosis. Women with a partner were 1.97 times more likely to desire children than other women.

4. Many of these factors for which African women differ from other women, for example partnership status, partners HIV status and age at diagnosis, may

affect fertility decision-making. Adjustment of neonatal seroprevalence data will therefore be stratified by ethnicity.

5. Sixteen percent of HIV-positive women had had a pregnancy subsequent to their diagnosis and this was related to decision-making at the time of their diagnosis.

Section 6b: Generalisation of survey findings

6B.1: Introduction

The generalisability of results from the questionnaire study to the HIV-positive population at large depends on how representative the study cases were of all diagnosed HIV- positive women in the population. This section presents results from analyses comparing women participating in the survey with that of all diagnosed prevalent HIV infections amongst women (Survey of Prevalent HIV Infections Diagnosed (SOPHID)). In addition, characteristics and pregnancy history of women participating in the questionnaire study were compared with women surveyed through the National Study of Sexual Attitudes and Lifestyles (NATSAL) to assess possible fertility differences between HIV positive women and a general population of all women whose HIV status was unknown. Finally, limitations of the survey are discussed.

6B.2: Comparison of survey population with all HIV-positive women

The demographics of the HIV-positive women participating in the survey were compared with that of all diagnosed prevalent HIV infections amongst women in GB in 2002 using a chi-square statistic. The 2 groups were compared in terms of drug use, ethnicity and age group, factors collected in both surveys. Women in the survey resident in Scotland were not included in this analysis as SOPHID data was not collected.

Eight thousand nine hundred and sixty-seven women received HIV-related care in England, Wales and Northern Ireland in 2002. Of these women, 393 (4.4%) were surveyed in the questionnaire for the purposes of this thesis. Survey women were more likely to be of black African ethnicity than all HIV-positive women (Table 6.10) and this reflects the higher sampling of clinics in the London area. The oversampling of African women will improve the interpretation of survey data as it is has been well documented that African women are more likely to have babies and are therefore more likely to be in included in neonatal prevalence data. Importantly, no apparent differences were found in the age distribution of women sampled through the questionnaire and all diagnosed HIV-positive women. Childbearing is strongly associated with the woman's age, thereby making age an important factor to take into account when understanding fertility-decision making amongst women.

Table 6.10: Comparison of survey women with all diagnosed prevalent HIV infections amongst women in England

	Survey women	SOPHID (2002)	P value
No. of women	393	8967	
History of IDU			
Yes	19 (5%)	290 (3%)	
No	369 (95%)	8675 (97%)	0.07
Ethnicity			
Black African	307 (78%)	6205 (69%)	
Black Caribbean	14 (4%)	297 (3%)	
White	48 (12%)	1663 (19%)	
South Asian	9 (2%)	103 (1%)	
Other	15 (4%)	278 (8%)	0.003
Age Group			
15-24	22 (6%)	713 (8%)	
25-39	268 (71%)	5735 (66%)	
40-49	87 (23%)	1800 (26%)	0.16

6B.3: Comparison of survey women with all women surveyed through NATSAL

To help understand the effects of HIV on fertility, the characteristics, including fertility history, of survey women and women surveyed through NATSAL (a population-based survey carried out in GB) were compared. Women from NATSAL were assumed to be HIV-negative, a reasonable assumption given that HIV prevalence amongst women in GB is low. The methodology for NATSAL was described in chapter 3 whilst the characteristics of NATSAL women were analysed in chapter 4. The variables used to compare the groups of women were: Residence, age group, ethnicity, marital status, previous pregnancies and dates of previous pregnancies, previous miscarriages and terminations, periods of infertility and whether the woman had received help for infertility. In total there were 461 African and 10,343 non-African women surveyed through NATSAL.

The ethnic distribution of HIV-positive women compared to women whose HIV status was unknown was different. Of the 450 HIV-positive women in the survey, 19.3% were White, 2.0% were Asian, 3.1% were black Caribbean, 72.0% were black African and 3.5% other. The equivalent figures in NATSAL were 91.7% White, 2.9% south Asian, 2.0% black Caribbean, 1.1% black African and 2.4% other. These discrepancies reflect the increased risk of HIV infection amongst black African women and, to a lesser extent, black Caribbean women.

Compared to women whose HIV status was unknown and regardless of ethnicity, HIV-positive women were older, less likely to be married, more likely to be single and less likely to have 3+ children (Table 6.11).

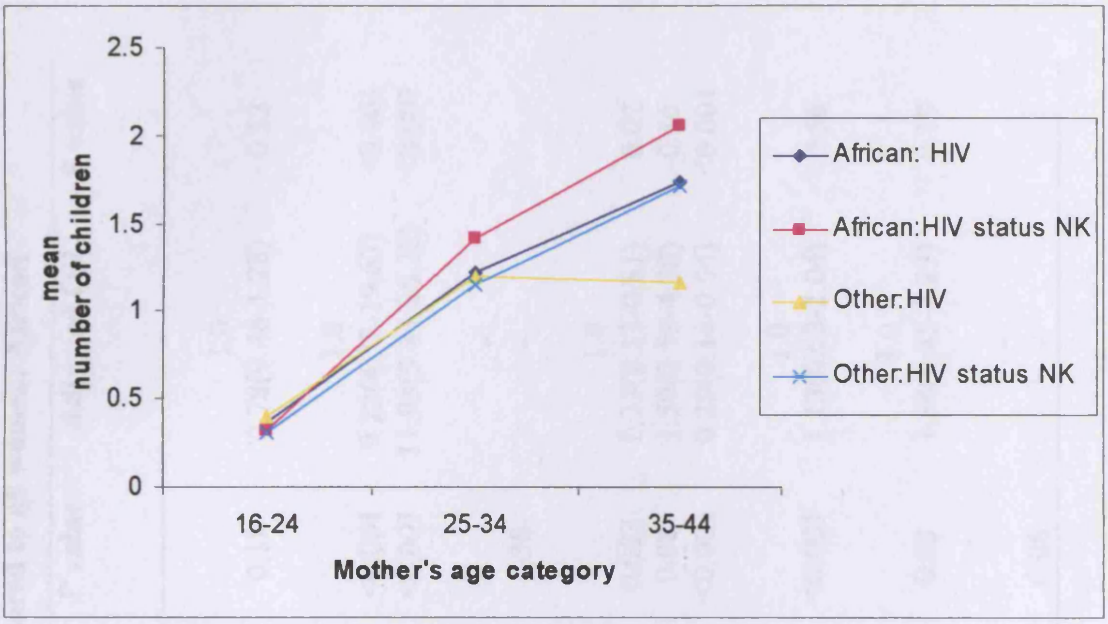
Table 6.11: Comparison of NATSAL women to survey women

	African women			Other women		
	NATSAL (%)	Survey (%)	P value	NATSAL (%)	Survey (%)	P value
Age group						
16-24	18.5%	6.1%		25.8%	4.1%	
25-34	40.0%	43.2%		37.5%	33.3%	
35-44	41.5%	50.6%	0.004	36.7%	62.6%	<0.001
Partnership status						
Married	44.6%	26.9%		44.6%	23.8%	
Div/sep.	15.4%	11.4%		7.2%	13.5%	
Widowed	1.5%	10.2%		0.3%	5.6%	
Single	32.3%	45.4%		29.4%	38.9%	
Co-habit	6.2%	6.2%	0.010	18.4%	18.3%	<0.001
No. children						
0	30.8%	25.0%		40.3%	34.1%	
1	16.9%	29.0%		17.5%	28.6%	
2	20.0%	25.6%		25.9%	24.6%	
3+	32.3%	20.4%	0.050	16.3%	12.7%	0.013
Ever miscarriage						
Yes	31.7%	17.6%		20.7%	23.8%	
No	68.3%	82.4%	0.012	79.3%	76.2%	0.42
Ever termination						
Yes	38.5%	23.8%		16.6%	33.3%	
No	61.5%	76.2%	0.011	83.4%	66.7%	<0.001
Trying preg 6 mths						
Yes	12.3%	24.9%		16.2%	14.1%	
No	87.7%	75.1%	<0.001	83.8%	85.9%	0.56
Sought help infertility						
Yes	6.3%	11.3%		9.1%	8.9%	
no	93.7%	88.7%	0.25	90.9%	91.1%	0.92

Whilst African HIV-positive women in the survey were less likely to have had a previous miscarriage or termination of pregnancy and more likely to have been trying for a pregnancy for greater than 6 months than African women whose HIV status was unknown, the reverse was true when other HIV-positive women were compared to other women whose HIV status was unknown. Data on miscarriages and terminations of pregnancy should be interpreted with caution as it was apparent from the questionnaire returns that many women confused these terms.

As HIV-positive women were significantly older than the general population, they would be expected to be more advanced in their child-bearing decisions. The mean number of children for each group of women was compared, stratified by age group (Figure 6.4). African HIV-positive women had a lower mean number of children than all African women at all age groups and this was most apparent in women aged 25 years and over. Other HIV-positive women had similar mean number of children at ages 16-34 years, but lower number of births at age 35 and over.

Figure 6.4: Mean number of children by HIV status, ethnic status and age category



The association of a previous live birth and HIV infection was investigated further using logistic regression. After adjustment in the model for factors significant in univariate analysis (age group, residence, partnership status, previous miscarriage, previous terminations and medical help for fertility), HIV-positive women regardless of ethnicity were less likely to have had a previous live birth than other women, although this was not statistically significant (OR 0.78, 95% CI 0.48-1.28, p=0.331 for African women and OR 0.66, 95% CI 0.40-1.08, p=0.097 for non-African women) (Table 6.12 and 6.13). These results agree with other studies that compared pregnancy rates before and after HIV diagnosis and found that after HIV diagnosis women were less likely to become pregnant (68, 92- 93).

Table 6.12: Likelihood of a previous livebirth in HIV-positive women compared to all women: African

	Previous live birth N (%)	Total n (% of N)	Crude OR	P value	Adjusted OR	P value
HIV status						
HIV status NK	190 (41%)	461	1.0		1.0	
HIV positive	162 (41%)	394	0.99(0.67-1.45)	0.18	0.78(0.48-1.28)	0.33
Age group						
16-24	13 (17%)	78	1.0		1.0	
25-34	142 (42%)	335	11.14(5.60-22.13)	<0.001	9.22(4.32-19.67)	<0.001
35-44	189 (45%)	421	17.58(8.79-35.13)	<0.001	11.93(5.43-26.22)	<0.001
Residence						
London	286 (41%)	702	1.0		-	
Outside London	66 (43%)	152	1.43(0.84-2.43)	0.38	-	
Partnership						
Married	127 (46%)	276	1.0		1.0	
Co-habiting	20 (37%)	54	0.25(0.11-0.56)	0.002	0.33(0.13-0.81)	0.02
Div./Sep./Wid.	92 (45%)	206	1.79(0.69-4.64)	0.08	1.59(0.59-4.28)	0.16
Single	112 (34%)	327	0.19(0.11-0.32)	<0.001	0.29(0.16-0.54)	<0.001
Previous miscarriage						
No	258 (40%)	642	1.0		1.0	
Yes	91 (44%)	205	1.93(1.17-3.20)	<0.001	1.13(0.63-2.04)	0.56
Previous abortion						
No	231 (40%)	573	1.0		1.0	
Yes	119 (43%)	276	1.50(0.98-2.31)	0.03	1.38(0.85-2.23)	0.19
Medical help						
No	316 (42%)	761	1.0		-	
Yes	29 (37%)	78	0.59(0.32-1.08)	0.06	-	

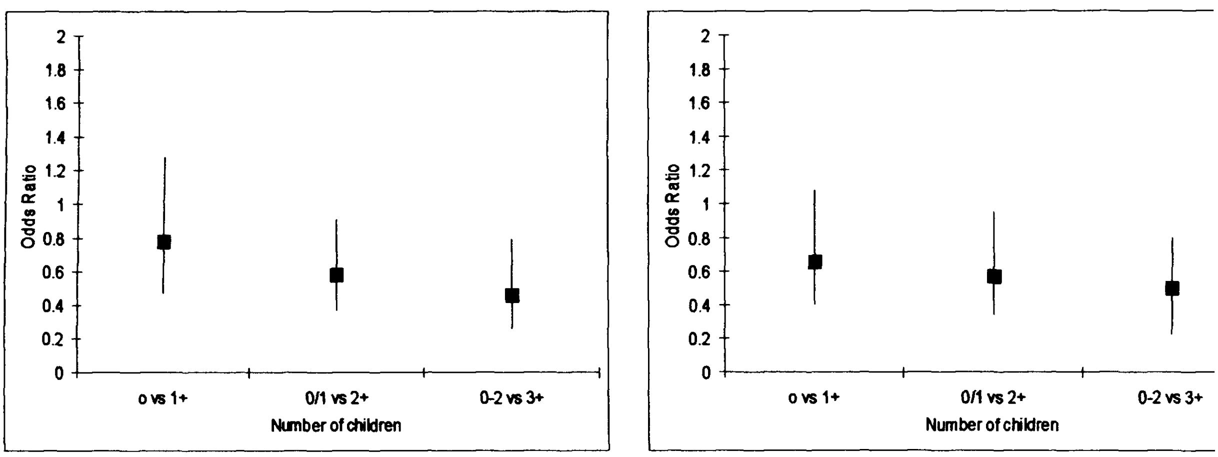
Table 6.13: Likelihood of a previous livebirth in HIV-positive women compared to all women: Non-African

	Previous live birth n (%)	Total N(% of n)	Crude OR	P value	Adjusted OR	P value
HIV status						
HIV status NK	3882 (38%)	10,343	1.0		1.0	
HIV positive	47(35%)	135	0.76(0.50-1.16)	0.19	0.66(0.40-1.08)	0.09
Age group						
16-24	326(18%)	1783	1.0		1.0	
25-34	1578(38%)	4158	5.46(4.72-6.33)	<0.001	2.43(2.05-2.87)	<0.001
35-44	2022(45%)	4530	14.43(12.32-16.91)	<0.001	4.86(4.04-5.87)	<0.001
Residence						
London	779(34%)	2269	1.0		1.0	
Outside London	3150(38%)	8209	1.51(1.34-1.69)	<0.001	1.61(1.39-1.86)	<0.001
Partnership						
Married	2149(46%)	4715	1.0		1.0	
Co-habiting	547(35%)	1562	0.23(0.19-0.27)	<0.001	0.30(0.25-0.36)	<0.001
Div./Sep./Wid.	612(46%)	1332	1.13(0.89-1.43)	0.29	1.05(0.82-1.35)	0.22
Single	620(22%)	2865	0.07(0.06-0.09)	<0.001	0.14(0.12-0.16)	<0.001
Previous miscarriage						
No	2690(35%)	7781	1.0		1.0	
Yes	1175(46%)	2554	5.14(4.39-6.02)	<0.001	3.47(2.89-4.15)	<0.001
Previous abortion						
No	3023(37%)	8282	1.0		1.0	
Yes	844(41%)	2058	1.69(1.48-1.93)	<0.001	1.57(1.35-1.85)	<0.001
Medical help						
No	3439(37%)	9301	1.0		1.0	
Yes	429(41%)	1039	1.67(1.39-2.00)	<0.001	0.63(0.50-0.78)	<0.001

The association of previous live births and HIV status was also analysed by comparing HIV-positive and HIV-status unknown women with none versus 1+, <2 versus 2+ and <3 versus 3+ live births. The purpose of this analysis was to assess whether or not HIV infection was associated with birth order. After adjustment, multivariate logistic regression showed that the association of fertility with HIV infection increased with higher birth order (Figure 6.5). Diagnosed HIV-positive African women were 0.46 (OR 0.46, 95% CI 0.26-0.79, p=0.005) times less likely to have 3+ children than other African women. HIV-positive non-African women were 0.50 (OR 0.50, 95% CI 0.22-0.80, p=0.039) times less likely to have 3+ children than other non-African women. These results may suggest that whilst HIV-positive women do have children, fertility is reduced or delayed.

Figure 6.5: Adjusted Odds ratios'* comparing the likelihood of a diagnosed HIV-positive Woman versus an HIV-status unknown woman having children

African women | Other women



*Adjusted for age group, partnership status, residence, ever had a miscarriage or terminations, ever received help for fertility.

6B.4: Limitations with survey methodology

A major strength of the cross-sectional questionnaire study was the direct measurement of fertility decisions in a sample of HIV-positive women. However, a number of limitations to the interpretation of results should be noted.

- The overall sample size was sufficient and came within the original sample size calculation conducted at the beginning of the study. However, once results were stratified by different demographic factors, numbers were small in some cells. This may have led to non-significant results.

- Whilst the study looked at desire for children, data was not collected on whether women achieved or thought they would achieve their desires. Whilst pregnancies subsequent to HIV diagnosis were explored, many of the women had been diagnosed within the previous 2 years, and so had not been given the chance yet to achieve their fertility potential.

- Birth rates among HIV-positive women in this survey were unknown, precluding a comparison to rates amongst the general population.

- The terms termination of pregnancy and miscarriage were often misunderstood by participants, limiting the usefulness of these variables.

- Many of the women participating in the survey were recent immigrants to the UK and had unresolved asylum status. Due to the sensitivity of this issue, a direct question on asylum status was not requested on the questionnaire. This factor could not therefore be included in analyses.

- Many HIV-positive women in GB are diagnosed due to routine antenatal HIV screening. This may mean that if a woman has become pregnant she will be more likely to be diagnosed, possibly leading to an overestimate of fertility in this survey population.

- The cross-sectional questionnaire survey provided an important insight into reproductive-decision making amongst HIV positive women, although some important issues which had not been included in the questionnaire, for example partner's desire for children, may have been under-estimated. Whilst a more qualitative approach to the questionnaire would have given a better insight into childbearing decisions, this approach was not utilised in this thesis as data from a representative sample of women was required for the final model. The development of the questionnaire however would have benefited from a focus group analysis.

- The questionnaire was undertaken among a heterogenous population where English was often not the first language. Validation of responses to the questions would therefore have been useful and would have confirmed whether or not the questions had been interpreted correctly. Validation could have been carried out using a focus group analysis or by asking a sample of women to complete the questionnaire twice.

- Current CD4 count was not found to be significantly related to reproductive decision-making. An alternative measure of well-being may have been CD4 count at diagnosis or lowest ever CD4 count

6B.5: Key Points

1. HIV-positive women sampled through the survey were representative of all diagnosed HIV-positive women in terms of age. This is important when studying fertility decisions.

2. Compared to all women, HIV-positive women were older, less likely to be married, more likely to be single and less likely to have 3+ children.

3. HIV-positive women were less likely to have had a previous live births than all women, although this difference was not significant (OR 0.78, 95% CI 0.48-1.28, p=0.331 for African women and OR 0.66, 95% CI 0.40-1.08, p=0.097 for non-African women).

Chapter 7: Estimating HIV prevalence amongst women in the general population in GB from neonatal seroprevalence data

7.1: Introduction

In many countries, including GB, HIV prevalence estimates among women are based on the observed prevalence amongst pregnant women (4,58). This estimation assumes that HIV-infected women have an equal probability of being pregnant than uninfected women (7). However, on the one hand women born in SSA have both higher HIV and fertility rates than other women (chapter 4), while on the other hand there is some evidence to suggest that HIV infection can impair female fertility or the ability to have a successful pregnancy (chapter 6), which would mean that HIV-infected women maybe less likely to become pregnant or to have a live birth. This means that neonatal seroprevalence, the commonly used measure in GB of HIV prevalence among pregnant women, needs to be adjusted taking into account the fertility differences between HIV-positive and HIV-negative groups.

The results from the investigations presented in chapters 4-6 were used in the final stage of the project to develop a model which would enable the extrapolation of neonatal prevalence data to give reliable estimates of HIV in the general female population. This chapter begins with a summary of factors affecting interpretation of neonatal prevalence which the adjustment model will need to account for. The model developed for this project is then described, together with a description of parameter estimation, results and validation analyses.

7.2: Summary of factors affecting interpretation of neonatal HIV prevalence

Analyses in chapters 4-6 showed the following factors affected child-bearing and HIV prevalence, which in turn affect the interpretation and extrapolation of neonatal seroprevalence. In summary:

- Women born in SSA have higher overall fertility rates and a higher HIV risk than women born elsewhere.
- Women in urban areas, for example London, are at higher risk of HIV infection than those in more rural areas. This is unrelated to their country of birth.
- Both total number of children and HIV prevalence are associated with age.
- Knowing ones HIV positive status leads to a reduced desire for children, resulting in the fertility of women who know themselves to be HIV positive to be lower than what it would have been based on cultural/ethnic factors.
- The number of children a woman has had at the time of HIV diagnosis was strongly associated with future reproductive-decision making.

These factors therefore should be included in any model which extrapolates neonatal seroprevalence data to the general population. To quantify the effect of each variable for use in the model, the following is needed: fertility relative to a reference group, HIV prevalence and the population size. Analyses in chapter 4 provided the HIV prevalence and population size data whilst the results from logistic regression models from the survey presented in chapter 6 provided the fertility measures.

7.3: Estimates of HIV amongst women in the General Population using neonatal seroprevalence data

The number of diagnosed and undiagnosed HIV infections amongst women in the general population in a given year was estimated using a model consisting of 2 separate components (Figure 7.1). The first component comprised of women aged 15-44 years who were at risk of having a live birth, thereby likely to appear in the neonatal surveys. The second component consisted of women who were not at risk of having a live birth, either because they were not of child-bearing age (45 years and over), they had never wanted to have any children or they had completed their family prior to their HIV diagnosis. This model was repeated for 4 separate years (1997, 2000, 2001 and 2002) to assess changes over time and to validate the model.

Figure 7.1: Overall model to estimate HIV amongst women in the general population

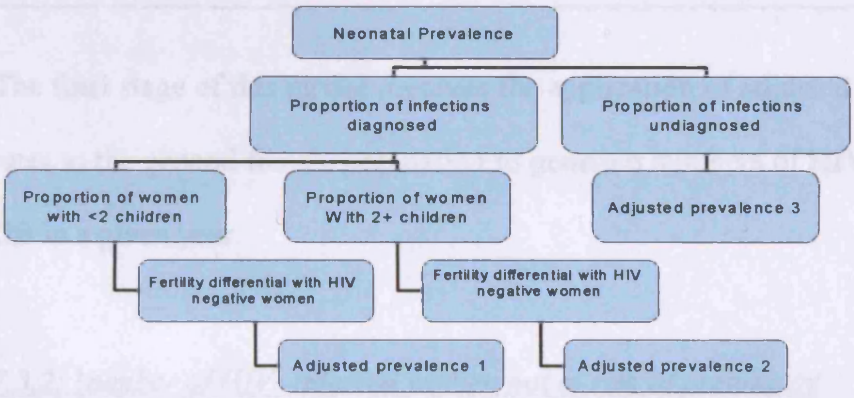
Number of HIV infected women in the general population	=	Number of HIV infected women at risk of pregnancy **(component 1)**	+	Number of HIV infected women not at risk of pregnancy **(component 2)**

7.3.1:Number of HIV-infected women at risk of pregnancy using neonatal seroprevalence data

The first component of the model was based on neonatal seroprevalence data. For a woman to be picked up in neonatal seroprevalence surveys, she has to become pregnant and have a live birth. From analyses in chapter 6 it was apparent that the diagnosis (ie. knowledge) of HIV infection reduced the likelihood of a woman having a live birth and that this reduction in fertility was dependent on the number of children the woman had already at the time she was diagnosed. This effect may be termed fertility differential. It was assumed that an undiagnosed HIV-infected woman would not intentionally reduce her fertility. Any reduction in fertility in this group of women would therefore be unintentional and this was assumed to be extremely low and was therefore not included in the model.

Based on this information, neonatal seroprevalence was stratified by whether or not the woman was born in SSA, area of residence (London versus rest), whether or not infection was likely to be diagnosed and, for women with diagnosed infection, the number of children they had had at the time of diagnosis. Prevalence rates were then adjusted for differences in fertility risk between HIV-positive and HIV-status unknown women. Figure 7.2 shows the detailed structure of component 1 of this model.

Figure 7.2: Structure of model to estimate number of HIV-infected women at risk of pregnancy (Component 1)



In mathematical terms, for each stratified prevalence:

Let P=Neonatal HIV seroprevalence

D=Proportion HIV infections diagnosed

U=Proportion HIV infections undiagnosed (or 1-D)

A=Proportion of women with <2 children at time of HIV diagnosis

B=Proportion of women with 2 or more children at time of HIV diagnosis (or 1-A)

F1=Fertility differential in women after HIV diagnosis in women with <2 children

F2=Fertility differential in women after HIV diagnosis in women with >=2 children

Prevalence in women at risk of pregnancy =Adjusted prevalence 1 + Adjusted prevalence 2 + Adjusted prevalence 3

= ((P*D*A*F1) + (P*D*B*F2) + (P*U))

The final stage of this model involves the application of adjusted neonatal prevalence rates to the general female population to generate numbers of HIV infected women in GB in a given year.

7.3.2: Number of HIV- infected women not at risk of pregnancy

The second component of the model, which relates to the number of diagnosed and undiagnosed HIV infected women not at risk of having a live birth, included women who were 45 years and older, women who had already completed their family size at diagnosis and women who never wanted children regardless of their HIV status.

These parameters were estimated using results presented in chapters 5 and 6. Analyses in chapter 5 provided data on numbers of diagnosed prevalent HIV infections according to age category whilst analyses in chapter 6 provided information about child-bearing history at time of diagnosis. Older women and women who never wanted children contributed to both a diagnosed and undiagnosed fraction of the model. In order to be consistent with component 1, results were stratified according to risk, residence and whether or not the woman had been diagnosed.

In mathematical terms, for each stratification:

Let: A=Number of HIV-infected women aged 45 years and over (Diagnosed)

B= Number of HIV-infected women aged 45 years and over (Undiagnosed)

C=Number of HIV-infected women aged 15-44 who have completed their family at time of diagnosis (diagnosed)

D=Number of HIV-infected women aged 15-44 who never wanted children (Diagnosed)

E=Number of HIV-infected women aged 15-44 who never wanted children (Undiagnosed)

No. of women not at risk of pregnancy=A+B+C+D+E

The estimated numbers from component 1 and 2 were then added together to provide an overall estimate (diagnosed and undiagnosed) of the number of HIV infections amongst women in GB in a given year. Finally, the age-specific numbers of infections among women in GB were generated by applying the age distributions of diagnosed

HIV-infected women reported to SOPHID to the estimated number of infections among women generated by the model.

7.4: Parameter Estimation for numbers of HIV infections amongst women

In summary, the following parameters were needed for the model:

- Neonatal seroprevalence by risk (whether or not the woman was born in SSA) and area of residence (Component 1)
- Proportion of infections diagnosed by risk, area of residence and age (Component 1 and 2)
- Proportion of HIV-positive women with <2 children at time of diagnosis by risk and area of residence (Component 1)
- Fertility differential between diagnosed HIV-positive and HIV- negative women by risk, residence and number of children at time of diagnosis (Component 1)
- Age-distribution of neonatal prevalence (Component 1 and 2)
- Population estimates for women by risk and residence and age (Component 1 and 2)
- Number of HIV-positive women 45 years and older by risk and residence (Component 2)
- Proportion of HIV-positive women who have completed family at diagnosis (Component 2)
- Proportion of HIV-positive women who never wanted children (Component 2)

The following section describes how the parameters were estimated and which results will be used in the final model.

7.4.1: Neonatal HIV seroprevalence

Overall neonatal HIV prevalence, adjusted for areas not included in the UA programme, was derived for 2002 in analyses in chapter 4. This analysis was repeated for 1997, 2000 and 2001 for use in the model and results are shown in Table 7.1 with 95% confidence intervals. Prevalence was highest in London among women born in SSA, and levels of HIV have risen from 1.49% in 1997 to 2.32% in 2002. Whilst rates in the other group were substantially lower, prevalence has also increased over time (Table 7.1).

Table 7.1: Neonatal HIV Prevalence by residence and risk, adjusted for areas not included in the UA programme

		HIV Prevalence (%) (95% confidence intervals)			
		1997	**2000**	**2001**	**2002**
London	**SSA**	1.494 (1.490-1.498)	1.887 (1.880-1.894)	2.222 (2.215-2.229)	2.316 (2.309-2.323)
	Other	0.042 (0.041-0.042)	0.049 (0.048-0.050)	0.064 (0.063-0.065)	0.062 (0.061-0.063)
Rest GB	**SSA**	0.652 (0.649-0.655)	1.068 (1.058-1.078)	0.991 (0.981-1.000)	1.367 (1.356-1.377)
	Other	0.0096 (0.0095-0.0096)	0.013 (0.013-0.014)	0.015 (0.014-0.015)	0.019 (0.019-0.020)

7.4.2: Proportions of HIV infections diagnosed

It is important to estimate the proportion of infections amongst HIV-positive women diagnosed as an HIV diagnosis was shown to affect subsequent desire for children (chapter 6). Proportion diagnosed was estimated by comparing the number of women diagnosed prior to pregnancy reported to the National Study of HIV in Pregnancy and Childhood (NSHPC) with the number of seropositive neonatal samples estimated from the unlinked anonymous surveys (Chapter 3). This comparison works on the principle that the neonatal seroprevalence survey collects data on all infections amongst women having live births, whether diagnosed or undiagnosed, whilst the

NSHPC collects data only on diagnosed and reported infections. Only women diagnosed prior to pregnancy were included so as not to bias the results with increased number of reports detected as a result of antenatal screening. Both the NSHPC and the neonatal seroprevalence survey collected information on mother's country of birth, mother's area of residence and year of child's birth.

Table 7.2 presents the results from this analysis for 1997 and 2000 to 2002. The proportion of infections diagnosed has increased between 1997 to 2002 in all groups of women, possibly reflecting improvements in HIV testing services (30). Between 2000 and 2002 the proportion of diagnosed infections amongst women within London increased significantly (p=0.003 for women born in SSA and p<0.001 for other women), and separate yearly rates will therefore be included in the model. For women resident outside London, where lower numbers of infections were observed, no significant change between 2000-2002 was observed and therefore an average yearly proportion will be included in the model.

Table 7.2: Estimated proportion of diagnosed HIV infections among women

		% (no. of reports from NSHPC/no. of positive neonatal samples)*			
		1997	**2000**	**2001**	**2002**
London	**SSA**	20% (40/196)	42% (107/255)	43% (130/299)	52% (174/334)
	Other	39% (15/38)	21% (9/43)	61% (39/64)	51% (34/67)
Rest GB	**SSA**	16% (7/45)	49% (39/80)	46% (47/102)	47% (71/152)
	Other	25% (13/53)	39% (32/82)	27% (25/94)	32% (41/128)

*0.8% of reports from the NSHPC and 11% of HIV positive neonatal samples had missing information on mother's country of birth. These cases were therefore proportionally distributed across the table.

7.4.3: Fertility differential between diagnosed HIV-positive and women whose HIV status was unknown

The final parameter needed for component 1 of the model was the fertility differential for HIV-positive compared to HIV-negative women. The fertility differential in HIV-positive women compared to HIV-negative women has previously been termed the Relative Inclusion Ratio (RIR) (60), the relative probability of including HIV-infected and uninfected women in a seroprevalence survey. This differential is equivalent to the ratio of live birth rates in HIV-infected women to live birth rates in uninfected women (see below formula). Once this differential is obtained, the prevalence in the population group of interest can be estimated as the prevalence observed among pregnant women multiplied by the differential. Fertility differentials were described in more detail in chapter 2.

$$\text{Fertility differential} = \frac{\text{P (HIV +ve)}}{\text{P (HIV –ve)}} \sim \frac{\text{P (live birth inHIV +ve)}}{\text{P (live birth in HIV-ve)}}$$

Based on results from chapter 6 a fertility differential was estimated for HIV-positive women, according to whether or not the woman wanted children after diagnosis, whether the woman was born in SSA, was resident in London or elsewhere and whether or not the woman had <2 children at diagnosis. Women with >=2 children were expected to have little HIV-related fertility decline as they had been diagnosed later in the course of their infection. The influence of improvements in HIV management on trends in HIV prevalence were investigated as part of a detailed sensitivity analysis (section 7.6).

One third of women did not want children after their HIV diagnosis and two thirds of these women had <2 children at time of diagnosis. For the model, it was assumed that women who did not want further children after their HIV diagnosis would indeed not have any more children. Therefore the mean number of children they had already had at time of diagnosis was estimated and divided by the number of children one would expect these women to have, (2.51 for women born in SSA and 2.1 for other women, published data from the General Household Survey on number of children a woman expects to have in her lifetime) (150), to provide a fertility differential. It was assumed that the remainder of diagnosed HIV- positive women who stated an HIV diagnosis had had no effect and HIV-positive women who were unaware of their infection would have a fertility differential of 1.0, i.e. their fertility would be unaffected by their HIV status.

When stratified by country of birth and whether or not the woman had had <2 children at diagnosis, the fertility differential for women who no longer wanted children after diagnosis was substantially lower in women with <2 children (range

0.18-0.23) while, as expected, nearly 1 in women with >=2 children (range 0.88-1.0) (Table 7.3). The overall fertility differential for all diagnosed HIV-positive women was significantly smaller than 1 (0.79 in women resident in London and 0.80 in women resident elsewhere), which confirms a trend of decreased fertility in the HIV-infected group. Few differences were observed between women born in SSA and women born elsewhere and between women resident in London compared to other women. These results support the argument that the effect of an HIV diagnosis decreases the total number of children a woman will have and that they will therefore be less likely to appear in neonatal seroprevalence surveys than other women. The effect of this is that if neonatal seroprevalence data are not adjusted for a fertility differential amongst HIV- positive and HIV-negative women, the number of infections amongst the general population will be underestimated.

7.4.4: Estimating number of women aged >=45 years

The number of women aged 45 years and above with a diagnosed HIV infection was obtained from SOPHID. The number of undiagnosed women aged 45 years and above was estimated assuming the proportions presented in Table 7.2 for HIV-positive women aged 15-44. This may be an underestimate, as older women may be more likely to have their infection diagnosed if they have been infected longer, have had more time to develop symptoms and have had more opportunities to have been in contact with health care services. This was not accounted for in the model as the consequence of this underestimate would be expected to have a small effect on the overall results.

Table 7.3: Estimation of fertility differential in diagnosed HIV-positive women

		Women who did not want children at time of their HIV diagnosis (3% of cohort of women)[3]				All diagnosed HIV positive women
		Women with <2 children (70% of cohort of women)[4]		Women with >=2 children (30% of cohort of women)[4]		
		Mean no. of children at diagnosis[5]	**Fertility differential[1]**	**Mean no. of children at diagnosis[5]**	**Fertility differential[1]**	**Overall fertility differential[2]**
London	**SSA**	0.46	0.18	2.25	0.90	0.79
	Other	0.28	0.13	2.01	0.96	0.79
Rest	**SSA**	0.58	0.23	2.22	0.88	0.80
	Other	0.45	0.21	2.14	1.00	0.80

1 For example, for women born in SSA & resident in London the fertility differential=mean no. of children at diagnosis divided by expected no. of children gathered by the general Household Survey =0.46/2.51

2 For example, for women born in SSA & resident in London the overall fertility differential=(0.18*0.34*0.70) + (0.90*0.34*0.30) + (1.0*0.66). It was assumed women who did not want children after their HIV diagnosis (34% of cohort of women) would have the reduced fertility differential as estimated in the table according to number of children at time of diagnosis and that women who said HIV had not affected their decisions (66% of cohort of women) had a fertility differential of 1.0

3 Data analysed from question 26 of the questionnaire survey

4 Data based on proportion of women with <2 children or 2 or more children interviewed in the questionnaire survey. These results were similar to data obtained from new HIV diagnoses (CDSC reports) and reports of HIV infected pregnant women (ICH reports).

5 Mean number of children at diagnosis amongst HIV positive women participating in the questionnaire survey

7.4.5: Estimate of the number of HIV-positive women who had completed family size at the time of their diagnosis

Results from chapter 6 indicated that 17% of African women and 13% of other women had completed their family at the time of their HIV diagnosis. These proportions were therefore applied to SOPHID data to estimate overall number of women aged 15-44 who would not appear in neonatal surveys because they had already had their children at the time of their HIV diagnosis. Newly diagnosed HIV infection reports received at CDSC were assessed to determine what proportion of women had had 2 or more children at time of diagnosis and whether this had changed over time. Results showed that between 2000-2002 16% of African women and 11% of other women had had 2 or more children and that this had not changed during the time period studied, which is in line with our estimates used from the questionnaire survey.

7.4.6: Estimate of the number of HIV-positive women not wanting children

Results from chapter 6 showed that 1.8% of African women and 4.8% of other women never wanted children, regardless of their HIV status. These proportions were applied to SOPHID data to estimate number of women aged 15-44 who would not appear in neonatal surveys. The number of undiagnosed women was estimated using the proportions diagnosed presented in Table 7.2.

7.5: Results: Number of HIV infections in women in the general population

Estimates of numbers of infections amongst women are presented in Table 7.4. More detailed results are presented separately in Appendix G including a working example of how the data for the model were generated. Ninety-five percent confidence intervals are provided for totals which allow for uncertainty regarding the neonatal seroprevalence. Uncertainties regarding assumptions made throughout the modeling analyses are explored in a sensitivity analysis.

In 2002, an estimated 16,120 (15,790-16,450) women were living with HIV, of whom 6210 (38%) were unaware of their infection. Numbers of infections have risen 2.5 fold between 1997 and 2002, and this rise was most marked in diagnosed infections. The rise in numbers of infections likely reflect improvements in HIV testing services, increased awareness about the benefits of getting tested, continuing migration between countries with high HIV prevalence and the UK and the decline in HIV-associated deaths since the introduction of more effective therapies.

The age-specific estimated number of infections among women in GB for 2002 are shown in Table 7.5. It was assumed the age distribution was the same for diagnosed as well as undiagnosed infection. The majority of infections were amongst women aged 25-34 years. Few women aged under 20 were infected with HIV, whilst there is an increasing prevalence of infected women aged above 45 years . Older women with HIV is having an increasing importance over time, as survival in women increases with advancements in therapies.

The model has provided a point estimate of number of infections amongst women in a given year using neonatal seroprevalence data. Deaths and HIV-infected women emigrating from the UK has not therefore been included in the figures as these women would have been unlikely to have had a live birth in that year. Whilst uncertainty remains about the level of emigration due to lack of available information, deaths among HIV infected women is now small in the era of HAART. The effect of these issues is addressed in chapter 8.

Table 7.4: Overall numbers of infections amongst women in GB*

		1997	2000	2001	2002
Diagnosed		*2690*	*6730*	*7910*	*9910*
London	**Women born in SSA**	920	2690	3250	4250
London	**Other**	860	1320	1690	1690
Rest GB	**Women born in SSA**	230	1460	1510	2180
Rest GB	**Other**	680	1260	1460	1790
Undiagnosed		*3890*	*4730*	*5510*	*6210*
London	**Women born in SSA**	1560	1680	2010	1940
London	**Other**	560	640	830	860
Rest GB	**Women born in SSA**	600	920	930	1300
Rest GB	**Other**	1170	1490	1740	2110
Total		**6580 (6480-6660)**	**11,460 (11,120-11,800)**	**13,420 (12,930-13,890)**	**16,120 (15,790-16,450)**

*All figures rounded to nearest 10

Table 7.5: Number of HIV infections amongst women by age category: 2002*

	Women born in SSA			Women born elsewhere			Total
	Diagnosed	**(%)**	**Undiagnosed**	**Diagnosed**	**(%)**	**Undiagnosed**	
<20	120	(1.9)	50	30	(0.9)	20	**220**
20-24	710	(11.0)	310	580	(16.7)	430	**2030**
25-29	2070	(32.2)	920	670	(19.3)	500	**4160**
30-34	2020	(31.4)	890	1200	(34.4)	890	**5000**
35-39	880	(13.7)	390	550	(15.8)	410	**2230**
40-44	90	(1.4)	40	30	(0.9)	20	**180**
45+	540	(8.4)	640	420	(12.1)	700	**2300**
Total	**6430**	**(100)**	**3240**	**3480**	**(100)**	**2970**	**16,120**

*Figures rounded to the nearest 10.

7.6: Sensitivity analyses

Sensitivity analyses were undertaken in areas of uncertainty surrounding the model to test the robustness of assumptions and to look at the effect of changes on prevalence estimates. Three different scenarios were considered:

1. Effect of changes in fertility differential between HIV-positive & HIV-negative women
2. Effect of changes in the estimate of proportions of infections diagnosed
3. Effect of changes in migration patterns on HIV prevalence estimates

7.6.1: Effect of changes in the fertility differential between HIV positive and HIV negative women

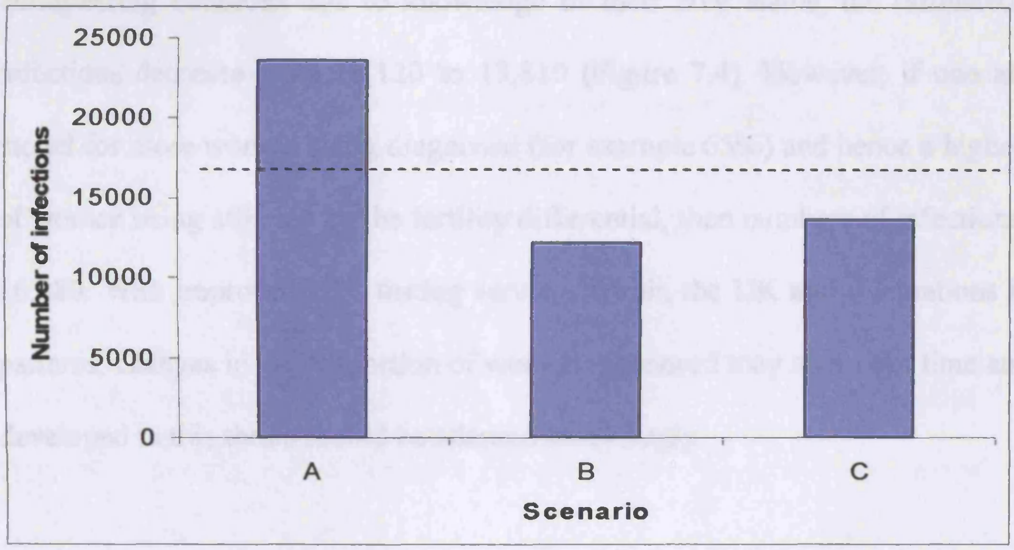
Fertility information used in the model was predominantly gathered as part of the questionnaire study, described and analysed in chapter 6 of this thesis. Whilst it was clear an HIV diagnosis had had an effect on intentional fertility decisions, assumptions were made in order to quantify the fertility differential between HIV-positive and HIV-negative women. A third of women stated that an HIV diagnosis had made them not want children anymore. Among the women who stated that their HIV diagnosis had had no effect on their childbearing intentions, at the time of the survey many HIV-positive women did not have a partner, many women were in a discordant relationship and uncertainties remained about asylum status. On the other hand it was clear from the questionnaire that recent improvements in HIV management had altered women's desire for children in that they now wanted more children which may in turn complicate the interpretation of trends in neonatal seroprevalence.

Three different scenarios were considered to explore uncertainty surrounding fertility amongst HIV-positive women. The first scenario (A) assumed that all HIV-positive women stop having children once they have had an HIV diagnosis, thereby applying the reduced fertility differentials shown in Table 7.3 to all women with an HIV diagnosis. The second scenario (B) assumed that an HIV diagnosis would not have any effect on subsequent childbearing, and hence all HIV-positive women would have a fertility differential of 1.0. The final scenario (C) considered women who had changed their fertility decisions in light of improvements in HIV management (14%) whereby these women were assumed to revert to having a fertility differential of 1.0.

The neonatal seroprevalence data for 2002 were adjusted assuming the above scenarios, and results are presented in Figure 7.3. If it is assumed all HIV-positive women no longer have children once an HIV diagnosis has been made (A) and a necessary adjustment is made for this, the number of infections estimated in the population would be 23,600. This is 47% higher than the 16,120 infections predicted. If however HIV-positive women are assumed not to be affected by their HIV status (B) and no adjustment is made to the prevalence data, 12,200 women would be estimated to be living with HIV in GB in 2002. This is an underestimate of 32% of that predicted by the model. Allowing for changes in response to improvements in HIV management (C) made a more modest impact on the difference in the estimated number of infections (13,720). This suggests that improvements in treatments and interventions in HIV management have probably had limited effect on the increasing seroprevalence seen amongst pregnant women since 1997 and that this rise is more likely to be attributed to changes in migrational patterns.

An additional factor to consider were women (16%) who stated in the questionnaire survey that an HIV diagnosis had made them want children sooner. Whilst these women would not have more children overall and therefore would not affect numbers of infections in a given year, they may affect trends as they would have their children over a shorter time span. This effect was not thought to be great and not therefore included in the sensitivity analyses.

Figure 7.3: Effect of changes in the fertility differential between HIV-positive and HIV-negative women on numbers of HIV infections



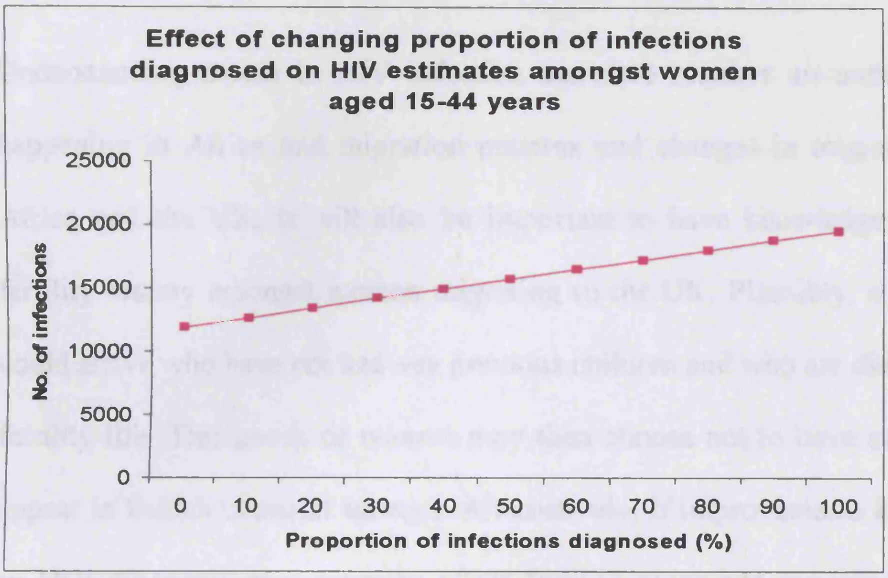
--------- Number of infections predicted in 2002

7.6.2: Effect of changes in the proportion of infections diagnosed

Estimating the proportion of infections diagnosed in a population is difficult without undertaking a population-based serosurvey. In this analysis, the proportion of infections diagnosed was assumed to be the same for all women as for women proceeding to birth who had already had their infection diagnosed regardless of the current pregnancy. However, this approach assumes women who become pregnant are representative of all women and women who do not get pregnant are excluded. An accurate estimate of proportion of infections diagnosed is important as that is the proportion of HIV-positive women to whom a fertility differential is applied to.

We originally assumed 32-52% of infections were diagnosed, dependent on country of birth and area of residence, but yearly fluctuations in this estimation were apparent. The effect of changes in the proportions of infections diagnosed was explored as part of the sensitivity analysis. If one allows in the model for fewer HIV-positive women being diagnosed (for example 25%) and thereby a lower proportion of women altering their childbearing decisions due to knowledge of their HIV status, the estimated number of infections decrease from 16,120 to 13,810 (Figure 7.4). However, if one allows in the model for more women being diagnosed (for example 65%) and hence a higher proportion of women being affected by the fertility differential, then numbers of infections increase to 16,880. With improved HIV testing services within the UK and fluctuations in migration patterns, changes in the proportion of women diagnosed may alter over time and the model developed in this thesis should be adapted accordingly.

Figure 7.4: Effect of changes in the proportions of infections diagnosed amongst HIV-positive women



7.6.3: Effect of changes in migration patterns on HIV prevalence estimates

The majority of newly diagnosed HIV infections in GB are amongst women born in sub-Sahara Africa, reflecting close links between Africa and the UK and the higher HIV prevalence rates in African countries. Updated HIV prevalence estimates have recently been published for Africa (15), with estimates for the overall adult population ranging from 1% in Western Africa to 39% in Southern Africa. The course of the HIV epidemic within GB has been and will in the future be dominated by what is happening in Africa.

The largest African community within the UK are women born in Nigeria, however due to the low HIV prevalence rate throughout Western Africa, people originating from Nigeria have not featured that widely in the UK HIV epidemic to date. Instead the majority of new HIV infections in the UK up until the early 1990's were associated with Uganda, a country with an HIV prevalence rate of 5%. More recently however the majority of new infections have been attributed to recent migration from Zimbabwe, a country where HIV prevalence is estimated to be much higher at 38%. The rise since 1997 of HIV infections in the UK corresponds to the rise in migration patterns of people from Zimbabwe to the UK.

Understanding trends in HIV infection therefore requires an understanding of what is happening in Africa and migration patterns and changes in migration patterns between Africa and the UK. It will also be important to have knowledge of age structure and fertility history amongst women migrating to the UK. Plausibly, a new wave of women could arrive who have not had any previous children and who are diagnosed earlier in their fertility life. This group of women may then choose not to have any children and never appear in British neonatal surveys. Alternatively, if improvements in treatments continue, an HIV diagnosis may cease to affect fertility plans and the importance of applying a fertility differential to neonatal seroprevalence data will diminish although ethnicity would still need to be adjusted for.

The effect on HIV estimates of a high proportion of women from Africa arriving in GB in the middle of their childbearing years, having previously had live births outside GB which would not have appeared in the British neonatal surveys was explored. It has earlier been shown that approximately 70% of women born in SSA had less than 2 children at time of diagnosis. Of these women, 38% of women had had no children at all and therefore could potentially have their full childbearing years in GB, and thus would not affect prevalence results. Forty five percent of women had had 1 child outside GB at diagnosis, thereby reducing their expected number of children (or alternatively live births which would have been picked up by neonatal screening) in GB from 2.5 to 1.5 and having a fertility ratio of 0.6 compared to other women. Finally sixteen percent of women had had 2 children outside GB at diagnosis, thereby reducing their expected number of children in GB from

2.5 to 0.5 and having a fertility ratio compared to other women of 0.2. The overall effect on the fertility ratio for women born in SSA would be 0.69 ((0.45*0.6) + (0.16*0.2) + 0.38). An additional application of this ratio to seroprevalence data amongst women born in SSA and resident in London would change the estimated number of infections form 3250 to 4710. This analysis confirms the importance of the inclusion of parity in the final model and highlights the necessity of monitoring fertility patterns in women migrating to GB and women newly diagnosed with HIV infection.

7.7: Validation of model

The ideal way to validate the model described in this chapter would be to compare the HIV estimates amongst women, with female prevalence from a population prevalence survey (71- 72). However, population surveys are not available for Great Britain.

A different approach of validating the model is to compare the prevalence estimates with the estimated number of diagnosed women from SOPHID, which collects data on numbers of HIV infected persons receiving HIV-related care in a given year.

The estimated number of diagnosed infections generated in this thesis was higher than that estimated by SOPHID, particularly for women resident in London (Table 7.6). There are two possible explanations for the discrepancy. SOPHID data refer to HIV infections amongst black Africans whereas the data in this thesis is for women born in SSA. This discrepancy is likely to be minimal as the majority (98.5%) of HIV-positive black African women were born in SSA and few (1%) of HIV-positive women born in SSA were not of black African ethnicity (ref unpublished data, CDSC). The second and more likely explanation for the difference is that it has been acknowledged that SOPHID data underestimates numbers of diagnosed prevalent infections for women by approximately

2.5 to 0.5 and having a fertility ratio compared to other women of 0.2. The overall effect on the fertility ratio for women born in SSA would be 0.69 ((0.45*0.6) + (0.16*0.2) + 0.38). An additional application of this ratio to seroprevalence data amongst women born in SSA and resident in London would change the estimated number of infections form 3250 to 4710. This analysis confirms the importance of the inclusion of parity in the final model and highlights the necessity of monitoring fertility patterns in women migrating to GB and women newly diagnosed with HIV infection.

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13% due to under-reporting (134). After this underestimate to the SOPHID total has been accounted for in this analysis, the total number of diagnosed infections estimated by the 2 methods were comparable.

Table 7.6: Comparison of number of diagnosed prevalent infections derived from SOPHID and the Model for all women in GB: 2002

		SOPHID	Adjusted SOPHID[2]	Model
London	Born in SSA[1]	3730	4210	4250
	Other	1330	1500	1690
Rest GB	Born in SSA[1]	2130	2410	2180
	Other	1590	1800	1790
Total		**8780**	**9920**	**9910**

[1] SOPHID data relates to African women
[2] Data adjusted for under-reporting and diagnosed HIV-positive persons not accessing HIV-related care

Whilst it is relatively easy to validate diagnosed HIV estimates, validating undiagnosed estimates is more problematic as less is known about the spread of undiagnosed HIV infection in GB. Compared to undiagnosed estimates produced by the direct method, the number of infected women produced by our approach was higher (6210 compared to 4600) (Table 7.7). The direct approach uses neonatal and STD clinic attenders seroprevalence rates applied to population data to estimate numbers of infections amongst women. The method used in this thesis uses neonatal seroprevalence rates and adjusts these rates for a fertility differential between HIV positive women and all women and has accounted for women who would not appear in neonatal surveys because they were not at risk of pregnancy.

Table 7.7: Comparison of undiagnosed estimates with HPA Direct estimates for 2002

	Direct estimates		Model Estimates	
	Diagnosed	**Undiagnosed**	**Diagnosed**	**Undiagnosed**
Born in SSA	6800	2300	6430	3240
Other	3000	2300	3480	2970
Total	**9800**	**4600**	**9910**	**6210**

In summary, the 16,120 (15,790-16,450) HIV infections estimated amongst women in 2002 using the methodology developed in this thesis appears a plausible estimate and can be used as an improved approach to the direct method when estimating HIV amongst women. Results from sensitivity analyses indicated that the number of infections could be as high as 23,000 if the fertility differential used in this thesis was underestimated. In order to be valid, estimates need to be repeated on a yearly basis in order to accommodate any changes in the HIV epidemic within GB. The adaptability of this method to other countries, however, would depend on the availability of HIV surveillance data, population data and information regarding fertility amongst the HIV-positive population.

7.8: Key points

1. A model was developed to quantify and interpret the HIV epidemic amongst women in GB. This model provided a point prevalence estimate of HIV amongst women, using neonatal seroprevalence and other data sources. It was estimated that approximately 16,000 women were living with HIV in GB in 2002. This is a significant rise since 1997, when an estimated 6,500 women were living with HIV
2. Adjustment of neonatal seroprevalence data for a fertility differential between HIV- positive and HIV-negative women had a substantial effect on the unadjusted prevalence. For example, without adjustment an estimated 12,200 persons were HIV infected in 2002, increasing to 16,000 once an adjustment factor had been applied.
3. The estimates produced by the model were comparable with previous estimates of diagnosed infection provided by SOPHID. The number of undiagnosed infections estimated by the model was, however, more than that previously estimated using a direct approach (6,200 compared with 4,600). This discrepancy is due to improved methodology in this thesis.
4. HIV estimates were sensitive to the following factors: proportion of infections estimated to be diagnosed (13,810 – 16,880), fertility differential between HIV-positive and HIV-negative women (13,000 – 23,000) and changes in migration patterns between GB and countries with high HIV prevalence rates.

Chapter 8: Extrapolation of neonatal seroprevalence data to the general female population in GB: conclusion and way forward

8.1: Summary of main findings

Neonatal seroprevalence data has been extensively collected throughout GB since the early 1990's (50). Whether or not this data can be used directly to estimate numbers of HIV infections among all women depends on fertility being independent of HIV status (7). There are a number of reasons why this is unlikely to be the case and whilst any associations between fertility and HIV do not invalidate the production of HIV estimates, they do indicate that extrapolations of neonatal seroprevalence to all women should be cautious. The differences between neonatal and population seroprevalence could be relatively small, however the denominators to which seroprevalence rates are applied are extremely large, and a small difference in HIV seroprevalence between neonates and the general female population could result in a substantial underestimate or overestimate of the total numbers infected. It is therefore important to develop an approach of using neonatal seroprevalence data which incorporates adjustment factors for differential fertility between persons at varying HIV risk.

Whilst information was available prior to this project on HIV levels amongst neonates, little was known about reproductive-decision making amongst HIV-positive women in GB other than the apparent decline in live births after diagnosis (68,92-94). As this is important information required for the extrapolation of neonatal seroprevalence data to the general population, this area of research was addressed in detail in a cross-sectional questionnaire study which provided a unique opportunity to ask HIV-positive women about their desire for children and whether their decisions had been affected by their HIV diagnosis. The timing of this study was opportune in relation to recent changes in the management of HIV, for example advancements in HIV therapies (152), a reduction in vertical transmission rates (34-35) and initiatives to improve HIV diagnosis (46), factors which could be expected to influence a woman's desire for children. Analyses throughout this thesis also took advantage of multiple existing data sources in various ways, including improved demographic data collected with neonatal seroprevalence results, recently published 2001 census of population data and fertility history information collected on new diagnosis reports amongst HIV positive women.

The factors identified which would influence the usage of neonatal seroprevalence data in estimating numbers of HIV infections amongst all women are shown in Table 8.1. Adjustment for these factors produced plausible numbers of HIV infections amongst women which were higher than previously estimated in GB with an approach not adjusting neonatal data for differential fertility and HIV risk. Individually, each factor described in Table 8.1 was shown to have a different effect on the numbers of infections derived and it should not therefore be assumed that seroprevalence among neonates will universally underestimate or overestimate population seroprevalence. The data here indicate that in GB either could occur under plausible conditions. For example, one of the main factors associated with differing fertility and HIV risk was whether or not the woman had been born in SSA. Failure to adjust for this factor would lead to an overestimate of about 30% in numbers of infections amongst women if using neonatal seroprevalence data. On the other hand, survey results revealed that many women irrespective of ethnicity may experience a reduction in the number of live births after diagnosis, as has been shown previously, leading to an underestimate of infections (68,92-94). Whereas it has not been possible in other studies to investigate whether this decline is explained by knowledge of HIV status or other factors, in the study presented in this thesis for the one- third of HIV-positive women who decide they did not want children after their HIV diagnosis, this was most strongly dependent on number of children the woman had already had at time of diagnosis. Results from the questionnaire survey highlighted the fact that half the women who initially did not want children after their diagnosis went on to change their mind in light of improvements in HIV management, thus limiting the overall impact of knowledge of HIV status on future fertility decisions. Other analyses demonstrated that many HIV positive women have already had their children at time of diagnosis, would never have wanted children regardless of their HIV status or had aged out of their childbearing years and would therefore not appear in neonatal surveys. These factors were adjusted for in the final model.

Table 8.1: Potential biases in using HIV prevalence amongst neonates as an indicator of general female population prevalence

Factor likely to cause bias	Effect on HIV risk	Effect on fertility	Probable effect on prevalence in all women	Included in model
Born in SSA	+	+	Overestimate	Yes
Known HIV-positive status	N/A	-	Underestimate	Yes
Urban area of residence	+	+ or -*	Probably Overestimate	Yes
Older (>=25) women	+	+	Overestimate	Yes
<2 children at HIV diagnosis	NK	+ or -	Overestimate or underestimate	Yes
Married/Co-habit women	NK	+	Overestimate or underestimate	No
History of injecting drug use	+	-	Negligible effect	No

+ = Increased risk
- = Decreased risk
* Depending on country of birth

Another pattern of results which emerged from the analyses using routine population data sources was the more subtle importance of area of residence and age group, factors which would probably lead to an overestimate in number of infections if not accounted for when extrapolating neonatal seroprevalence data. Both women resident in London and older women were shown to have higher HIV infection rates and higher fertility patterns than other women. The increased HIV prevalence in London was predominantly attributed to the higher concentration of women born in SSA resident in that area, although HIV prevalence rates were still higher in London after adjustment for mother's country of birth.

In order to keep the model developed in this thesis as simple as possible, only factors considered easily quantifiable were incorporated. Two factors shown to be related to fertility and/or HIV risk but not included in the model were history of injecting drug use and partnership status. The biases associated with differential fertility amongst drug users have not previously been considered. Whilst fertility data were sparse, results indicated that IDUs were less likely to have a previous live birth than other women, more likely to have had a previous termination and more likely to have had a subsequent pregnancy after HIV diagnosis. However, analyses also indicated that drug users constituted a relatively small proportion of the British population and their HIV risk was relatively low compared to women born in SSA. Any bias associated with this group in estimating general population prevalence would therefore be limited.

Although partnership status was associated with desire for children and changes in desire in relation to improvements in HIV management, limited data were available on partnership and HIV risk and for this reason partnership was not quantified in the final model. Other studies have looked at the effect of partnership status amongst HIV-positive women on fertility decisions in detail and have found the relationship to be complex. Sherr et al found that partners, when present in clinic, were invariably involved and consulted in childbearing decisions (127). Kline et al found that it was the partner's desire for children that represented the determining factor for childbearing and that the respondents own desire for children had no direct effect (105). In our study, whilst partnership status played an important role in desire for children, partner's HIV status appeared not to be a significant factor. Over a third of women in a partnership were in a discordant relationship and in addition a substantial minority (16%) of women were unaware of their partner's HIV status, which could be suggestive of a lack of intimacy and possibly short duration of relationship.

Previous studies have found health status of the mother to be an important factor when making decisions about childbearing (106), although this was not the case in our survey. This was not surprising since most HIV-positive women are now less at risk of an AIDS-defining illness due to the availability of treatments than was previously the case. As expected, HIV-positive women of sub-Saharan African origin had had more pregnancies than other HIV-positive women at time of diagnosis. This finding was concordant with earlier analyses in the thesis using routinely available population data sources which showed that in GB fertility was higher in women born in SSA after adjusting for age. Race was not, however, a predictor for desire for children after diagnosis, a consistent finding from a previous study (125). This suggests that whilst women of African origin have more pregnancies than other women, the effect of an HIV diagnosis is similar for all women regardless of race.

Another question of interest throughout this thesis was the interpretation of the increase in neonatal HIV seroprevalence which has been recorded in all parts of GB since 1997 (30). It was unclear whether this rise corresponded to an increase in HIV in the general female population, or whether fertility decisions amongst HIV-infected women had changed due to improvements in the management of HIV infection, in which case the rise in prevalence could only be a temporary effect. Nearly half of the women who no longer wanted a child after their HIV diagnosis changed their mind once they had become aware of the improvements made in HIV management, confirming suggestions made by others of a relationship between altering fertility decisions and advancements in the natural history of HIV (99-100). Whilst women with less than two children were more likely to not want children after their HIV diagnosis, they were more likely to have changed their mind about wanting more children due to improvements in HIV management. This suggests that women who have not completed their family size at time of diagnosis are now more hopeful in the light of advancements in HIV therapies.

The overall proportion of women who did not want children after diagnosis but changed their mind in response to improvements in HIV management was modest (14% of the total cohort of women interviewed). Further analyses also indicated that women who did change their minds had not had significantly more pregnancies overall after their HIV diagnosis than other women. It was therefore considered unlikely that changes in childbearing intentions would have greatly impacted on the doubling of neonatal seroprevalence observed between 1997 and 2002 and that other factors such as migrational changes between GB and countries of high HIV prevalence were more likely to account for this rise.

Whilst in the survey many women reported to desire children, only 16% of them had had a pregnancy subsequent to diagnosis, thereby suggesting a discrepancy between desire and achievement. The questionnaire did not go into details about whether or not the woman was currently trying to conceive, so whilst she may have said she wants more children, she may not have currently been trying to achieve this. Secondly, a high proportion of the women included in the study had only been diagnosed within the previous 2 years and had therefore not yet been given a reasonable chance to become pregnant. However, it was also clear from the qualitative data collected in the survey that barriers were present which made childbearing difficult for this group of women. Many women had no partner and many of those who did have a partner were in a discordant relationship. A disproportionately large segment of those women affected by HIV were from minority groups, often financially disadvantaged with uncertainties regarding their asylum status in the UK. A study in England investigating the maternity experiences of asylum seekers (regardless of HIV status) found that many of the women in emergency accommodation were going hungry, no formula milk was being provided for the babies and little information about services and support was being given to them (153). A descriptive study of HIV positive African women living in London found that most had experienced very poor housing and financial conditions, many had been dependent on the National Asylum Support Service and almost half had been diagnosed because of ill health or the suspicions of a clinician (154). It is clear from these studies and the survey carried out in this thesis that whilst many HIV-positive women desire children, the contemplation of pregnancy is very difficult.

Nevertheless, results from separate analyses presented in this thesis using a national data source which included all reported diagnosed HIV pregnant women in GB but no qualitative information on decision-making did indicate that the proportion of HIV positive women with a subsequent live birth after their diagnosis has increased in recent years (24). This finding is consistent with observations from other studies in America (99-100) and Europe (155). The observed higher likelihood of having a subsequent birth to an HIV diagnosis during the era of HAART may be the result of a number of factors. Increased survival times for women with HIV as well as delayed progression to AIDS may result in greater opportunities to become pregnant. Alternatively, more women may be choosing pregnancy because of the lower risk of having a child with HIV infection. The proportion of pregnancies amongst women newly diagnosed during antenatal care ending in a termination has also declined dramatically from 2000 onwards, again suggesting that women diagnosed in the HAART era are increasingly willing to carry pregnancies to term.

In summary, many factors of differing influence were found to affect the validity of using neonatal seroprevalence data to estimate numbers of infections amongst the general population. The overall effect of these factors was an underestimate in the total numbers of infections amongst women. Whether or not the woman had been born in Africa was shown to be a bias associated with extrapolating neonatal seroprevalence data to population data and one which was easily adjusted for using population and surveillance data sources. The influence of differential fertility between HIV-positive and HIV-negative women on the HIV estimates was also considered important, although the bias associated with this may have been reduced by the fact that of the third of women who initially did not want a child after diagnosis, about half of these women later changed their mind in light of the improvements in HIV management.

8.2: Implications of findings

Overall, the results presented in this thesis suggest that data provided by seroprevalence studies amongst newborns in an attempt to estimate HIV prevalence amongst the general female population are more likely to have under-, rather than over- estimated the true number of HIV infections and that more accurate results could be generated using the method of adjustment described in this thesis. Rational decisions about health strategies and interventions need to be based on reliable and timely knowledge of the distribution of HIV infection, thereby necessitating the need for convincing estimates of HIV and the associated demographic, social and economic costs. During the time of this project the National Strategy for Health stated as one of its objectives the reduction in the numbers of undiagnosed HIV infections in the country (156). Data generated by this project could be used to monitor this objective amongst women, especially as estimates of undiagnosed infections could be repeated on an annual basis using updated surveillance data. In addition, a separate report by the Department of Health 'Getting ahead of the curve', which detailed a strategy to combat infectious diseases, emphasised the need for improving surveillance data in order that it gives a complete picture of the size and nature of the threat of infection (157). Again, the methodology developed in this thesis is in line with this objective.

Since it has been shown that neonatal seroprevalence is likely to underestimate HIV infection amongst women, alternative population groups could be considered , for example extension of surveillance programmes to include other groups of women, particularly those who do not become pregnant. Hospital patients have been used previously, although the absence of risk information with specimens has made interpretation of results problematic and these surveys have now been discontinued

(23, 158). HIV screening results from blood donations have also been suggested as a useful tool; however, results would be severely biased due to the difficultly in accessing population groups at highest risk of HIV coupled with active discouragement of people who perceive themselves to be at risk to donate blood. Therefore, usage of neonatal data remains the best approach to estimating HIV amongst women.

Results from this project also demonstrated that women with HIV do not rule out childbirth, an important consideration for health care professionals who treat HIV-positive women. Our finding that approximately 40% of diagnosed HIV-positive women desired children translates into over 3,500 positive women in GB who potentially will have a live birth in the next two years or so. In addition, many women with undiagnosed HIV infection are becoming pregnant and are increasingly likely to be diagnosed during antenatal care (46). HIV-positive women who desire children have numerous service needs in addition to the medical care needed for their own infection (105,125,127). To help make informed choices, family planning counselling and children of infected parents may need social service support (159). The desire for children also has implications for the transmission of HIV to partners and newborns. In the questionnaire survey a third of the HIV positive women who wanted children and were in a partnership had a partner who was HIV-negative or of unknown status. Women who give birth will require follow-up of the newborn until maternal antibodies disappear and HIV status can be ascertained (40). Whilst guidelines exist for the management of HIV infection in pregnant women (40), there are no established guidelines for defining access to fertility care for individuals infected with HIV and only a handful of in vitro fertilisation units in GB are prepared to treat couples if one or other partner tests positive (160). In the past the primary concern of fertility clinics has been the life expectancy of the infected parent, this is less justifiable in light of HAART and may now need to be re-considered, especially as the number of HIV-positive women is rising rapidly, the majority of women are within child-bearing age and without AIDS-related symptoms.

8.3: Limitations of data sources and analyses

Whilst the methodology developed in this thesis has undoubtedly improved HIV estimates among women, the results can only be as good as the data sources used and the appropriateness of the assumptions made. This section discusses the potential limitations of results and suggests areas for which improved information collection would benefit the reliability of the estimates.

8.3.1: Availability and Compatibility of information gathered from surveillance systems

A summary of the demographic information available from each of the routine surveillance data sources used in the analyses is shown in Table 8.2. Surveillance data always have limitations, for example records where information is missing. Ethnicity, country of birth and, in particular parity, was not reported or requested in a number of instances and it is difficult to know what effect this unavailability of information had on the overall results.

Information was derived from a number of different sources and the scope of analyses may have been limited by some issues of incompatibility between availability of ethnicity and country of birth information, overlapping but not identical categories (Table 8.2). The size of the Black African population in GB in 2002 was nearly 480,000 whilst the number of women born in SSA in GB was over 740,000. This discrepancy exists because many Africans were born in GB and many women born in SSA were of White or Asian ethnicity (census 2001 unpublished data).

When estimating numbers of HIV infections it is crucial to determine HIV prevalence rates by the correct risk factor, to apply these rates to the most appropriate population denominator and for definitions of population sub-groups to be consistent across the different data sources. If not, the number of infections may be over or under-estimated. Currently in GB, women born in SSA have a relatively high HIV prevalence whereas prevalence in the UK-born black African community is low (55). This data supports other evidence which shows the majority of HIV infection in women in GB is associated with time spent in Africa (26). The model developed in this thesis therefore categorised women according to their country of birth, a data item collected in all data sources except for the SOPHID survey. However, if appreciable changes in the HIV epidemic were to occur as the numbers of infections amongst migrants in GB continues to increase, ethnicity may become increasingly important. Unfortunately, this is a data item not collected in sufficient detail in the neonatal seroprevalence programme. Attempts have been made to improve capture of mother's ethnicity information with neonatal samples, although to date this has proved problematic with a large number of records having missing information (55).

Table 8.2: Summary of ethnicity, country of birth and parity information available through routine surveillance systems

Survey	Country of birth data	Ethnicity data	Parity data	Summary
Unlinked Anonymous neonatal seroprevalence survey	Collected for 3 regions in GB	Limited collection of maternal ethnicity in 1 region in GB between 1997 and 2001, affecting 56,000/640,000 births annually (55). Collection of child's ethnicity in 3 regions in GB	Not collected	Little demographic data collected outside London (29) In regions which collect country of birth, 6% of samples have missing information (29)
SOPHID: Survey of Prevalent Diagnosed HIV Infections	Not collected	Requested for all	Not collected	Missing ethnicity information on 4% of reports (Unpublished data, CDSC)
New HIV Diagnoses	Requested for all	Requested for all	Collected for 2000-2002	24% of reports have missing information on parity, 4% of reports miss country of birth and 1% of reports miss ethnicity (Unpublished data, CDSC)
NSHPC: Reports of HIV Infected Pregnant Women	Requested for all	Requested for all	Requested for all	Overall 31% of reports have missing information on parity, 18% of reports miss country of birth and 9% of reports miss ethnicity (Unpublished data, ICH)

8.3.2: Estimate of diagnosis rates amongst HIV-infected women

Results from sensitivity analyses in chapter 7 demonstrated that HIV estimates were sensitive to the proportion of infections assumed to be diagnosed. For example, if fewer HIV-positive women had been diagnosed than allowed in the model and thereby a lower proportion of women would have altered their childbearing decisions due to knowledge of their HIV status, the number of infections among all women would have been overestimated. The method developed in this thesis assumed that the probability of diagnosis in the whole female population was represented by the NSHPC data on numbers of diagnoses prior to the pregnancy. There are two reasons why this assumption may have under-estimated the true probability of diagnosis within the female population. Firstly, analyses from the survey showed that some diagnosed HIV-positive women no longer desired children after their diagnosis. Secondly, this approach fails to take into account the fact that women who had been pregnant in the previous year would have a higher probability of being diagnosed as a result of prenatal screening but a lower probability of being pregnant and thus reported in the NSHPC for the current year. The numbers of diagnosed infections estimated by the model did in fact correlate well with information deduced from other surveillance data sources. However, if alternative approaches to estimating the proportion of infections diagnosed were needed, the ideal source of information would be population-based serosurveys which included women who do not get pregnant. Information on whether or not the sample had been taken from a known infected person would also need to be collected, making this approach extremely difficult.

8.3.3: Representativeness of newborns included in the neonatal seroprevalence surveys

The unlinked anonymous neonatal survey is assumed to be population-based as it includes residual samples taken from virtually all neonates in GB who receive routine metabolic screening in the first week of life. It is reasonable to assume samples in the UA survey are representative of all samples taken from newborns as the objection rate for UA surveillance and the number of samples where insufficient residual blood is available for HIV testing after routine tests have been completed is extremely low (<1%) (23). However, selective under-coverage of babies born to women of black African ethnicity by routine neonatal screening has been suggested. The ratio of probability of black African women being included in neonatal screening in South East London to the ratio of all other women being included was found to be 0.97 (63). This could have implications for the UA surveys since HIV prevalence is higher among African women in GB suggesting that seroprevalence surveys may underestimate female population prevalence due to an under-representation of women at high risk of HIV infection. Further analyses by Hutchinson et al found that despite some selective under-representation, the results of the neonatal seroprevalence survey identified prevalence among childbearing women with a good degree of accuracy (62). These analyses were undertaken in 1996 and it is not certain whether any important changes have occurred since this research was undertaken. The recent introduction of assigning NHS numbers at birth and the continued enhancement of child health systems throughout GB may facilitate more research in this area. Birth registration records, which contain information about mother's country of birth, could be linked to neonatal laboratory records using the unique NHS number with a high degree of accuracy. This would enable identification of babies who have not undergone neonatal screening.

8.3.4: Generalisability of results from HIV positive women included in the cross-sectional questionnaire survey to all HIV positive women

The generalisability of results from the questionnaire study to the HIV-positive population at large depends on how representative the study cases were of all HIV-positive women in GB. A comparison of HIV positive women participating in the survey with all diagnosed prevalent HIV infections amongst women in England and Wales showed similar age distributions in both groups of women. As child-bearing is strongly related to age, this is an important finding when studying fertility decisions. However, it is known that a proportion of HIV positive women are not in HIV-related care (estimated at 5%) (134) and these women would therefore not have been sampled as part of the questionnaire survey. All the women in the study were outpatients and thus the views of severely ill women would not have been reflected in this study either.

It is also important to ensure that the HIV positive women in the questionnaire survey were representative of the population for whom HIV estimates are to be derived. For example, pregnant women would not be suitable as a source of fertility data as they would exclude infertile women. One concern was that the women participating in the questionnaire survey would be biased towards women who have previously been pregnant, as they are more likely to have been diagnosed following an HIV test as part of their antenatal care. Whilst this may have been the case, results indicated that the majority (70%) of women surveyed were not pregnant at the time of their diagnosis and would therefore have been diagnosed due to other reasons such as presence of HIV-related symptoms.

8.4: Future work

There are many ways analyses in this project could be developed further. This section discusses four different approaches: 1) Using results to estimate HIV prevalence amongst men, 2) Applying the model to different country settings, 3) Use of neonatal seroprevalence data for estimating incidence and 4) Developing the model further to predict and interpret changes in HIV prevalence over time.

8.4.1: Estimating HIV prevalence amongst men

The method developed in this project could be extended to estimate numbers of infections amongst men in the general population. This would involve generating an HIV male/female prevalence ratio and applying this ratio to the estimated number of infections amongst females. The current approach in GB ('Direct method') assumes the prevalence ratio in men is the same as in women (4-5). However, we know most heterosexually-acquired infections in GB are amongst Africans, that within Africa the prevalence ratio tends to be lower amongst men in the younger age groups and that variability in the ratio is dependent on individual country in Africa and severity of the HIV epidemic (28,161-162).

Historically, prevalence ratios in the developed world have been derived by using an AIDS incidence sex ratio (58). But, with the advent of new antiretroviral therapies few people now progress to AIDS, severely limiting the value of this method. The ratio of new HIV diagnoses amongst men compared to women has never been considered a suitable approach as the likelihood of an HIV diagnosis depends on perception of risk and whether or not someone has been offered an HIV test, factors which could differ between men and women. An alternative strategy would be to base an HIV prevalence ratio on knowledge of migration patterns of HIV-positive persons to GB and the HIV prevalence sex ratio in countries from which these persons have originated from. This would be the approach recommended based on results generated throughout this thesis, although current information on migration in GB is very limited.

8.4.2: Application of the model to countries outside GB to generate country-specific estimates

An additional application of this project could be to use the methodology to generate HIV estimates in other countries. The extrapolation from neonatal data to the adult population is based on assumptions that may not equally apply to all countries or at all times during the course of the epidemic. In GB, HIV prevalence was low and mainly restricted to certain risk groups such as migrants from high prevalence countries, about half the women were diagnosed, HIV-related treatment was readily available and there were low underlying patterns of fertility. The approach developed here would be most readily applied to other developed countries for example France with similar underlying HIV, migration and fertility patterns, depending on availability of neonatal seroprevalence data, fertility information on HIV-positive women and population statistics. Neonatal seroprevalence data is collected in France, however the usefulness of uding this data to generate estimates amongst all women in the general population has not been explored (personal communication, F Hammers).

In Africa, where the epidemic is more severe and accurate HIV estimates most needed, fertility and HIV patterns are different to those seen in GB. The majority of HIV-positive women are unaware of their infection, most HIV is heterosexually acquired, there are high underlying patterns of fertility among the population and HIV-related treatment is not readily available. In the African setting it is likely that any fertility differential between HIV-positive and HIV-negative women is attributable to biological or social factors rather than conscious decision-making. UNAIDS and WHO in collaboration with countries in Africa have already developed a six-step method to estimate HIV prevalence amongst adults. These estimates have been based on seroprevalence data derived from antenatal clinic attenders and adjust for representativeness of pregnant women who attend antenatal clinics, reduced fertility of HIV-positive women and under-representation of rural sites in surveillance systems (163).

8.4.3: Estimating incidence from neonatal seroprevalence data

Estimates of HIV incidence ("new infections") are rare as this data is difficult and costly to collect. Longitudinal cohort-based studies are required and these demand greater resources and organisation than cross-sectional studies used to obtain HIV prevalence data. Laboratory techniques have been developed which can identify blood specimens from individuals infected with HIV within the previous 6 months (164) and although costly these techniques can be extended to dried blood spots collected from neonates (165). However, this approach is only fully validated for testing specimens from HIV-infected individuals with subtype B (166), and previous studies in GB have shown that nearly 80% of HIV-positive pregnant women are a non-B subtype, reflecting the acquisition of HIV throughout Africa (167). This limitation is unfortunate because estimates of incidence rates can provide information on recent levels and patterns of infection. In contrast, prevalence data frequently reflects levels of infections over a period of many years, providing information which is already out of date when it is collected.

Previous studies in France and Africa have considered whether useful estimates of the incidence of infection can be derived from the readily available data on HIV prevalence (168-170). Incidence was estimated modelling age-specific prevalence data, accounting for mortality effects but not migration. The authors concluded the methods were useful in monitoring HIV infection and could be applied to data collected in other countries such as GB.

8.4.4: Predicting the course of the HIV epidemic over time

Whilst the model developed in this thesis provides a point prevalence estimate by year, the course of the HIV epidemic over time and the resulting estimates of incidence and mortality could not be evaluated. There are several factors which may affect the course or the description of the course of the HIV epidemic including:

1) The unknown duration of the effect of HAART in delaying death.

2) A change in the incidence of new infections in GB. Within GB the majority of new infections are now mainly confined to men who have sex with men, whilst transmission occurring within the indigenous heterosexual population is extremely small and stable (18). Most new HIV diagnoses among heterosexually infected individuals in GB are of long-standing infections acquired in Africa rather than

incident cases. Late diagnosis amongst Africans attending services in GB has been reported (149) and many of those diagnosed late have arrived in the country recently (26). However, this situation could change if the numbers of migrants continues to rise and the frequency of travel to countries with high HIV prevalence continues to increase.

3) A change in the movement of HIV infected people from Africa to GB. Major uncertainties remain over the future course of an epidemic dominated by infection probably acquired overseas. Knowledge of migration patterns of HIV-infected persons is crucial if the effect of this factor on HIV estimates in GB are to be interpreted with any certainty.

4) Increasing importance of non-African groups on the HIV epidemic in GB. Within Britain the size of population sub-groups born abroad and HIV risk of different groups is a changing dynamic. The majority of all women, regardless of HIV status, in this thesis were classified as Rest (ie. born outside SSA), a low HIV-risk category which includes an inhomogeneous group of women with a mixture of ethnicities and countries of birth. However the continuing influx of refugees and asylum seekers in GB could lead to a spread of HIV infection in groups from other areas outside of SSA, for example Eastern Europe (13), a region where HIV prevalence rates are rising sharply. The impact of the epidemic from countries such as Eastern Europe on migrant populations in GB should therefore be monitored closely, especially as the sexual mixing patterns amongst 'new' migrants may be different from behaviour patterns amongst more established migrants.

5) The effect of a policy of dispersal of new migrants to different parts of GB may affect the description of the course of the epidemic (13). The national policy of dispersal of refugees and asylum seekers could lead to a geographical spread of HIV throughout the country, with subsequent rises in neonatal seroprevalence outside London.

8) The proportion of HIV infections diagnosed amongst women may change, for example as a result of the promotion of HIV testing as recommended by the National Strategy for Sexual Health and HIV (156). Intended campaigns to enhance levels of diagnosis among women may lead to an apparent fall in the Relative Inclusion Ratio and thus the observed neonatal seroprevalence would decline even though there was no change in prevalence.

Work leading on from this thesis could be developed to monitor the course of the HIV epidemic taking the above factors into consideration. This would involve the development of a Markov Chain-based model which would analyze the changes of an individual through categories related to progression of HIV infection (171). Such a model would assume that an HIV-positive individual would start in an unrecognized state and gradually progress to a recognized state either due to HIV testing or development of HIV-related symptoms. Over time, HIV-positive women considered to be at risk of pregnancy will irreversibly progress to the stage of no longer being at risk of pregnancy. A proportion of new infections will occur each year, and a proportion of infections will pass to AIDS and possibly death. The changes in numbers of HIV infections in GB due to in-migration and out-migration would also be an important component of the model. Figure 8.1 illustrates the structure of such a model, which would need to be repeated for the 4 subgroups of women used in chapter 7; 1) Women born in SSA and resident in London, 2) Women born elsewhere and resident in London, 3) Women born in SSA and resident outside London, 4) Women born elsewhere and resident outside London.

The parameters estimated from the model developed in chapter 7 would create the starting point for this further work and would be defined as follows:

DR1=No. of diagnosed women with <2 children who are at risk of pregnancy

DR2=No. of diagnosed women with >=2 children who are at risk of pregnancy

D>45=No. of diagnosed women older than 45 yrs who are not at risk of pregnancy

DNR 15-44= No. of diagnosed women aged 15-44 who are not at risk of pregnancy

UR1= No. of undiagnosed women with <2 children who are at risk of pregnancy

UR2=No. of undiagnosed women with >=2 children who are at risk of pregnancy

U>45=No. of undiagnosed women older than 45 yrs who are not at risk of pregnancy

UNR 15-44= No. of undiagnosed women aged 15-44 who are not at risk of pregnancy

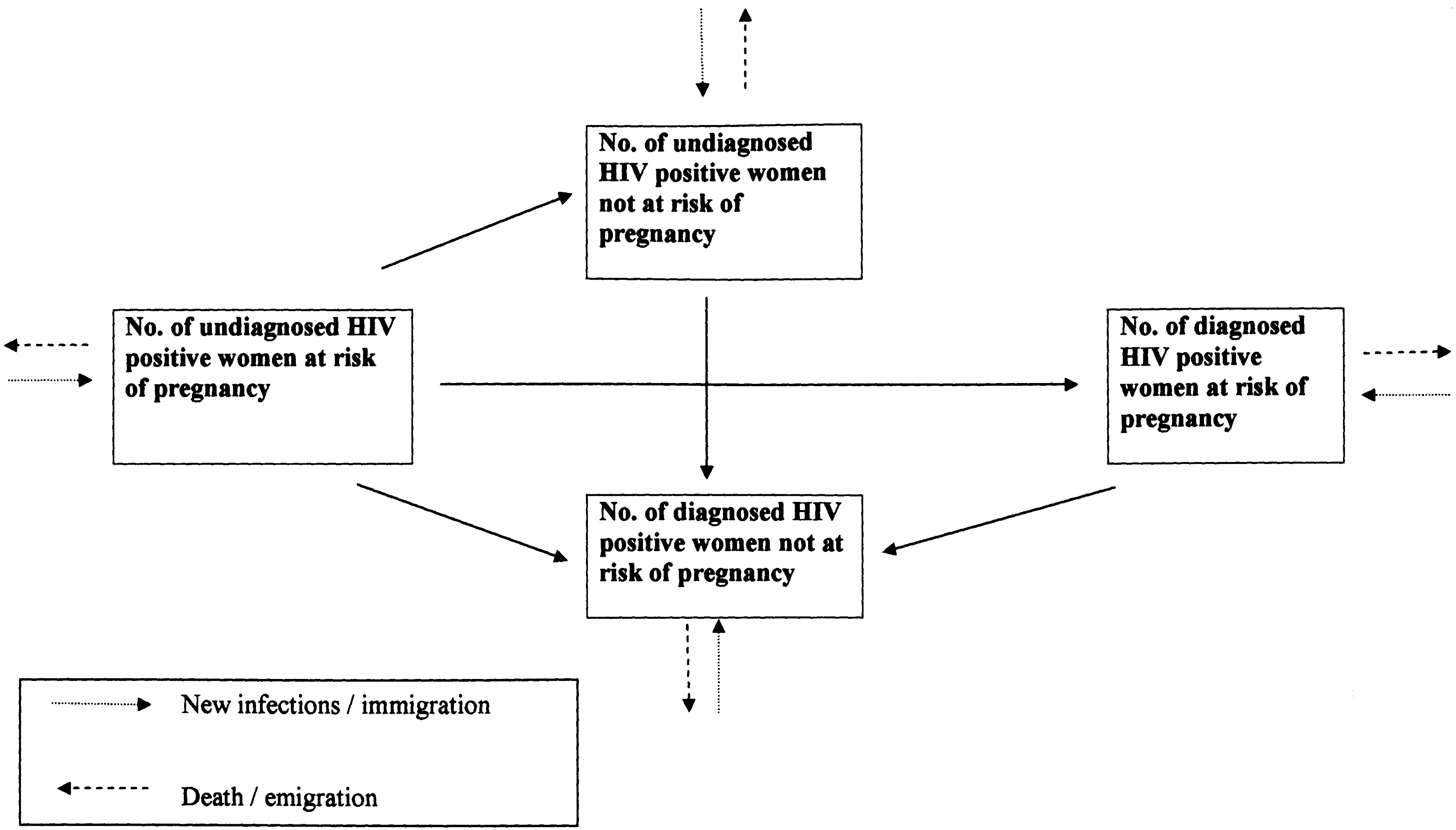
In addition to these estimates, the following information would be required:

Numbers of new HIV infections in a given year

Number of HIV-related deaths in a given year

Number of non HIV-related deaths in a given year

Figure 8.1: Structure of a model which could be used to monitor the course of the HIV epidemic in GB over time



The next stage would be the development of an "Allowed Transition Matrix". This is a matrix based on knowledge of the course of HIV infection and the likelihood of moving from one stage of infection to another. Table 8.3 gives an example of this matrix, where 1 indicates an allowed transition. For example, in a given year a diagnosed woman with <2 children (DR1) can either stay in that state or move to diagnosed with >=2 children (DR2), diagnosed >=45 years (DNR>45) or leave due to migration out of the UK or death. Once a woman is HIV infected she cannot move back to an uninfected state and once a woman is diagnosed she cannot move back to an undiagnosed state.

Table 8.3: Allowed transitions matrix

Link matrix	HIV-	DR1	DR2	D>45	DNR: 15-44	UR1	UR2	U>45	UNR: 15-44	Death/out migration
Recent arrival	1	1	1	1	1	1	1	1	1	1
HIV-	1	1	1	1	1	1	1	1	1	1
DR1	0	1	1	1	0	0	0	0	0	1
DR2	0	0	1	1	0	0	0	0	0	1
DNR>45	0	0	0	1	0	0	0	0	0	1
DNR:15-44	0	0	0	1	1	0	0	0	0	1
UR1	0	1	0	1	1	1	0	1	0	1
UR2	0	0	1	1	1	0	1	1	0	1
UNR>45	0	0	0	1	0	0	0	1	0	1
UNR:15-44	0	0	0	1	1	0	0	1	1	1

Estimates of the probabilities of transition across different HIV-related states in the model would then be defined. Much of the information required for this model is uncertain, thereby making sensitivity analyses crucial. Examples of how initial values required to estimate the transition probabilities could be generated are as follows:

Firstly, the movement of women in a given year between different HIV-related diagnosed states according to number of children and age (for example DR1 to DR2) may be based on data gathered on HIV-infected pregnant women reported to the NSHPC, analyses from the cross-sectional questionnaire survey showing proportions of women who never wanted or already had children at diagnosis and the age distribution of prevalent HIV infections diagnosed from SOPHID. Movement of women between undiagnosed states could be assumed to be either the same as in the corresponding diagnosed state or the same as HIV-uninfected women given that women who are unaware of their HIV status are less likely to change their childbearing plans because of their HIV infection.

Secondly, the transition of HIV from an undiagnosed to diagnosed state (for example UR1 to DR1) would need to be quantified. The majority of new HIV infections initially remain undiagnosed as testing is not undertaken on a regular basis and HIV-related symptoms only develop later in the course of infection. For the purposes of this model, it would be reasonable to assume that 10% of new infections will be diagnosed per year and that this is the same across all HIV states.

Thirdly, an estimate of numbers of new infections per year is needed (for example HIV negative to UR1). In women born in the UK incidence would be expected to be extremely low. However, in women born in Africa, the majority of new infections will equate to recently arrived HIV infected persons coming into the country who were infected elsewhere. This data could be estimated using reports of newly diagnosed HIV infections received at CDSC which contain information on year of arrival in the UK and fertility history.

Lastly, the risk of death could be derived from estimates of time of HIV diagnosis to death at different ages. These have already been derived in cohorts of HIV infected individuals in Europe, North America and Australia (152). Prior to widespread use of antiretroviral therapies, median survival rates were 12.5 years for persons aged 15-24 and 7.9 years for persons aged 45 and over. Since the use of therapies, death rates due to AIDS have fallen by 64%. It may be assumed that an HIV-infected woman with undiagnosed infection would have a death rate equivalent to that pre-HAART whilst a diagnosed HIV-infected woman would have a death rate equivalent to that since HAART has been made widely available.

Preliminary work which has used 2001 data to predict the course of the epidemic in 2002, and then compared the predicted values for 2002 with observed values for 2002, suggests that the model described has a reasonable fit. However, areas of uncertainty need to be addressed in order to refine the methodology. Whilst we are well informed about fertility patterns in different groups of women in GB, much less is known about migration patterns of HIV-positive persons in and out of the country and the effect of these patterns on the HIV epidemic in GB. The model depends on knowledge of HIV prevalence amongst migrants, according to age and sex. However, this data is not available and neither is it known how long migrants stay in the country. It is probably not reasonable to assume that the HIV prevalence in migrant populations is the same as that in the home country, as surveillance data indicate that whilst women resident in Zimbabwe have an HIV prevalence of about 30%, women born in Zimbabwe who have had a livebirth in GB have a prevalence much lower at 10%. Further development of this model depends on improved information on migration patterns, especially as any changes in HIV prevalence in countries within Africa are likely to be the major factor driving the course of the epidemic in GB.

8.5: Conclusions

An approach for improving HIV estimates among women in GB has been developed which can easily be updated on an annual basis using the adjustment factors derived in this project. This approach could be implemented using the routinely available data sources and the results of this thesis have been presented to both the HPA and ICH for consideration. Publication of findings will also be important. A primary aim of collecting sentinel unlinked anonymous prevalence data has been to monitor trends in HIV prevalence in the source population (2). The method developed here shows how this can be done, allowing for fertility and demographic changes in the population over time. The project demonstrates not only the importance of knowing fertility patterns amongst HIV-positive women, but also the requirement for more detailed demographic data on the British population. A large increase in numbers of HIV infections amongst women was shown to have occurred between 1997 and 2002 and this trend is likely to be attributed to migrational changes between the UK and countries of high HIV prevalence. However, the actual contribution of migration to numbers of infections is difficult to gauge in the absence of more detailed data on migrational patterns. Work furthering on from this thesis would be more complex modelling (which will experience difficulties in predicting migration) to improve our understanding of factors which are likely to drive the HIV epidemic in GB in the future.

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Appendix A: Interpreting neonatal HIV seroprevalence data in Great Britain: the importance of differential fertility

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Interpreting neonatal HIV seroprevalence data in Great Britain: the importance of differential fertility

S Cliffe, M Cortina-Borja, A Nicoll, M-L Newell

Appendix B1: Questionnaire used in survey of fertility decisions amongst HIV positive women

Clinic name: **Questionnaire number:**

Institute of Child Health *Health Protection Agency*

Study to understand the effect of HIV on pregnancy decisions

Thank you for giving up your time and agreeing to be part of this survey. This study is anonymous and none of the information provided will be communicated to anyone else. If the study has raised any concerns or questions you would like to discuss, please speak to your doctor or health advisor.

Study Address:

HIV & Fertility Study
Centre for Paediatric Epidemiology & Biostatistics
Institute of Child Health

SECTION 1: Questions 1-7 ask about you

1. What is your year of birth? ------------

2. Where do you currently live?

London ☐
Elsewhere in England & Wales ☐
Scotland ☐
Other ☐ ⟶ Please specify...........................

3. Were you born in the UK? Yes ☐ No ☐ If NO, Which country were you born? ---------------
What year did you arrive in the UK? ----------

4. What is your partnership status?

Single	☐	Widowed	☐
Married	☐	Cohabiting (living with partner)	☐
Divorced/separated	☐	Non-cohabiting partner (Regular partner but not living with them)	☐

5. Which ethnic group would you describe yourself as belonging to?

White	☐	Black African	☐
Black Caribbean	☐	Black Other	☐
Asian	☐	Other	☐

6. If you have a partner, what is their ethnic group?

White	☐	Black African	☐	Not Applicable	☐
Black Caribbean	☐	Black Other	☐		
Asian	☐	Other	☐		

7. Have you ever injected drugs?

Yes ☐ ⟶ If YES, have you injected in the last year? Yes ☐ No ☐
No ☐ ⟶

SECTION 2: Questions 8-14 ask about your HIV status

8. Please tell us the month and year of your first positive HIV test ---------(mth)---------(year)

9. Is your partner also HIV positive? *(tick one box only)*

Yes	☐	No	☐	Not applicable	☐
Not tested	☐	Don't know	☐		

10. How would you describe your current HIV symptoms? *(tick one box only)*

No symptoms ☐ Mild/moderate symptoms ☐ Severe symptoms ☐

11. Do you know your current CD4 count? Yes ☐ No ☐

If yes, in which category does it fall? <200 ☐ 200-349 ☐ 350-699 ☐ >=700 ☐

12. Has your CD4 count changed significantly in the last 6 months?

No ☐

Yes ☐ If yes, how has it changed? It has increased ☐ It has decreased ☐

13. Which describes your HIV therapy? (*tick one box only)*

Never on treatment ☐ Started treatment within past 3 months ☐

On treatment for more than 3 months ☐ Treated in the past but currently off treatment ☐

14. If on treatment, does your regime include:

1 drug ☐ 2 drugs ☐ 3 drugs ☐ 4 drugs ☐ 5+ drugs ☐ Not Applicable ☐

SECTION 3

We would now like to ask you some questions about pregnancies you have already had.

15. Are you or have you ever been pregnant? Yes ☐ No ☐ (*if NO please go to Section 4*)

16. Are you currently pregnant? Yes ☐ No ☐

17. Do you have, or have you had, any children? Yes ☐ (how many? ------) No ☐

If yes, please give year of birth for each child in the boxes below:

☐ ☐ ☐ ☐ ☐ ☐

18. If you have had children, are or were any of your children HIV positive?

Yes ☐ No ☐ Awaiting outcome ☐ Don't know ☐ Not Applicable ☐

19. Have you ever taken therapy during pregnancy to reduce the risk of having an infected child?

Yes ☐ No ☐

20. Have you ever had a pregnancy which has ended in any of the following:

	Number *(if none write '0')*	**Year(s)**			
a) Miscarriage	☐	☐	☐	☐	☐
b) Stillbirth	☐	☐	☐	☐	☐
c) Termination	☐	☐	☐	☐	☐

21. If you have ever had a termination of pregnancy (abortion), was the reason connected in any way to your HIV infection?

Yes ☐ No ☐ Not applicable ☐

22. Were you pregnant at the time your HIV was diagnosed? Yes ☐ No ☐

If YES, what was the outcome of that pregnancy?

Live birth (baby born alive) ☐ Still birth (baby died at delivery) ☐ Miscarriage ☐ Termination ☐

SECTION 4

We are very interested in knowing about how many (more) children you would like to have, and whether this has changed because of your HIV status

23. Would you like any (more) children?

Yes ☐ No ☐ Don't know ☐ I already have desired number of children ☐

24. Have you ever had a time, lasting 6 months or longer, when you and your partner were trying for a pregnancy but it did not happen?

Yes ☐ No ☐ Not Applicable ☐

25. Have you (or your partner) ever sought medical help about fertility?

Yes ☐ ⟶ If YES, are you currently receiving treatment? Yes ☐ No ☐

No ☐

26. Having had your HIV diagnosed did you change your mind about wanting (more) children?

I wanted children sooner ☐ I decided I didn't want children anymore ☐

I had already had my children ☐ My HIV diagnosis had no effect ☐

I never wanted children anyway ☐ Other .... ☐

27. Are you aware that treatments ('Combination therapy') for your HIV have improved recently and have made some people stay well? Yes ☐ No ☐

If YES, have these treatments made you feel better & changed your mind about wanting (more) children?

Yes they have made me feel better & want (more) children ☐

Always wanted (more) children anyway ☐

No they haven't made me feel better & want (more) children ☐

Never wanted (more) children anyway ☐

Other.. ☐

28. Are you aware that measures can be taken to help women reduce their chance of having a baby with HIV? Yes ☐ No ☐

If YES, have these measures have made you want (more) children?

Yes they have made me want (more) children	☐
No they haven't made me want (more) children	☐
Always wanted (more) children anyway	☐
Never wanted (more) children anyway	☐
Other………………………………………………	☐

29. Please provide the date you completed this questionnaire ……./………../…………..

30. Please provide any additional information about factors affecting your fertility decisions, for example your partner's feelings, immigration status, financial situation etc

Thank you very much for completing this questionnaire. Please put it in the envelope provided, seal it and either post it or hand it to the doctor/nurse/health advisor who asked you to participate.

Appendix B2: Information sheet used in survey of fertility decisions amongst HIV positive women

Institute of Child Health

Health Protection Agency

Study to understand the effect of HIV on pregnancy decisions

YOU ARE BEING INVITED TO TAKE PART IN A RESEARCH STUDY. PLEASE READ THIS INFORMATION SHEET BEFORE STARTING THE QUESTIONNAIRE

THIS STUDY IS STRICTLY CONFIDENTIAL

The aim of the study: A study among women is being carried out to understand how HIV affects pregnancy decisions.

Why is the study being done? We are keen to understand as much as we can about reasons for wanting children. You may be aware that there have been improvements in treatments that delay HIV disease and also improvements in measures to reduce the risk of a woman passing the virus to her child. We would like to know whether this has changed pregnancy decisions.

How is the study being done? All women attending clinic are being asked if they would like to take part in the study. If you agree, you will be asked to complete a questionnaire. It is important to stress that the study is completely confidential. We do not need your name or address and will collect nothing that identifies you. The questionnaire may be completed at clinic whilst you are waiting for your appointment or at home at a time convenient to you. If you take the questionnaire home a reply-paid envelope will be provided for returning the questionnaire.

The nurse or researcher involved with the study will be available if you would like to discuss any issues the study has raised.

Do I have to take part in this study? No. If you decide, now or at a later stage, that you do not wish to take part in this project, that is entirely your right, and will not in any way affect your care. If you have any complaints about the way in which this research project has been, or is being conducted, please, in the first instance, discuss them with the researcher.

Details of how to contact the Researcher: The researcher for this project is Susan Cliffe who can be contacted either by telephone on , or by post: Centre for Paediatric Epidemiology & Biostatistics, Institute of Child Health,

Finally, we would like to thank you for considering to take part in this survey.

Appendix B3: Consent form used in survey of fertility decisions amongst HIV positive women

STUDY TO UNDERSTAND THE EFFECT OF HIV ON PREGNANCY DECISIONS

Consent Form for PARTICIPANTS

NOTES FOR PARTICIPANTS

1. You have been asked to take part in some research. The person organising that study must explain the project to you before you agree to take part

2. Please ask the researcher or clinic nurse/doctor any questions you like about this project, before you decide whether to join in

3. If you decide, now or at any other time, that you do not wish to be involved in the research project, just tell us and we will stop the research. If you are a patient your treatment will carry on as normal

4. You will be given an information sheet which describes the research. This information is for you to keep and refer to at any time. *Please read it carefully*.

CONSENT

I .... agree that the research project named above has been explained to me to my satisfaction, and I agree to take part in this study. I have read both the notes written above and the information sheet about the project, and understand what the research study involves.

SIGNED	**PRINTED**	**DATE**
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Appendix C: List of Collaborators

Appendix D: European Collaborative Study Questionnaire

ECS3
INTENSIVE PROSPECTIVE STUDY OF CHILDREN BORN TO HIV POSITIVE MOTHERS

MATERNAL INFORMATION AT DELIVERY

Centre [ ][ ] 1-2
Mothers Study Number [ ][ ][ ] 3-5
Child Study Number [ ] 6
Mother's date of birth (day, month, year) [ ][ ][ ][ ][ ][ ] 7-12
Country of birth .... [ ][ ] 13-14

Marital Status
Single (1), Married (2), Divorced, Separated, Widowed (3), Cohabiting (4) [ ] 15

Ethnic Group
Asian (1), White (2), Black (3), Oriental (4), Other (5) [ ] 16
Age when leaving full-time education, years [ ][ ] 17-18

Obstetric History
Number of previous livebirths .... [ ][ ] 19-20
Number of previous stillbirths .... [ ][ ] 21-22
Number of previous miscarriages .... [ ][ ] 23-24
Number of previous terminations.. [ ][ ] 25-26

Mothers Risk Group
History of intravenous Drug Abuse (Y/N) [ ] 27
Trimester of last use: pre-conception (0), 1st (1), 2nd (2), 3rd (3), unknown (9) [ ] 28
Needle sharing? never (1) past (2) present (3) unknown (9) [ ] 29
Sexual partner of Bisexual (Y/N) [ ] 30
Sexual partner of Haemophiliac (Y/N) [ ] 31
Sexual partner of Intravenous Drug Abuser (Y/N) [ ] 32
Sexual partner of Other high risk group (Y/N) [ ] 33
(Specify) ....
Other :... [ ] 34

Mothers HIV History
Date of first HIV+ test (day, month, year) [ ][ ][ ][ ][ ][ ] 35-40

Current clinical status
Current HIV staging (CDC) .... [ ][ ][ ] 41-43
Specify symptoms .... [ ][ ][ ][ ] 44-47
Date of onset .... [ ][ ][ ][ ][ ][ ] 48-53

Details of antiretroviral therapy during pregnancy
Has the woman received any antiretroviral therapy at any time during this pregnancy?
If yes, please give details Y/N [ ] 54

Drug	Total daily dose	Date started	Date stopped	Currently taken? (yes/no)

[ ][ ] 55-56
[ ][ ][ ][ ][ ][ ] 57-62
[ ][ ][ ][ ][ ][ ] 63-68
[ ] 69
[8][1] 70-71

Appendix E: National Study of HIV in Pregnancy questionnaire

CONFIDENTIAL office use only

Tick boxes, complete, ring, or delete as appropriate week ___/___ [ ] [ ] *F1133*

Hospital ...*Newham*......... Your ref (eg woman's hospital number, local code or soundex) ....

Woman's date of birth ___/___/___ Previous livebirths .... stillbirths .... miscs/terms ....

Ethnic origin [ ] White [ ] Black African [ ] Black Caribbean [ ] Black other
[ ] Indian Subcontinent [ ] Oriental [ ] Other or mixed, specify ....

Country of birth................................ Current postcode of residence (leave off last letter) [ ][ ][ ][ ] [ ][ ][■]

PREGNANCY LMP ___/___/___

[ ] Continuing to term EDD ___/___/___

[ ] Spontaneous abortion *or* [ ] termination on ___/___/___ at .... weeks gestation

If spontaneous abortion or termination, any congenital abnormality? [ ] No [ ] Yes Please specify overleaf

Were antenatal booking bloods taken at this maternity unit? [ ] No [ ] Yes

PROBABLE SOURCE OF INFECTION

[ ] From high prevalence country, specify .... Date arrived UK/RoI ___/___/___

[ ] Injecting drug use [ ] Transfusion recipient [ ] Other, specify ....

[ ] Infected partner, specify his likely risk factor ....

HIV STATUS IDENTIFIED

[ ] During this pregnancy: voluntary antenatal testing / other setting, specify ....

[ ] Known prior to this pregnancy: tested at GUM Clinic / GP / Drug Clinic / other ....

Date of first positive test ___/___/______ If HIV-2 only, please tick here [ ]

HIV RELATED CLINICAL STATUS & DRUG TREATMENT DURING PREGNANCY

[ ] Asymptomatic [ ] Symptomatic, not AIDS [ ] AIDS diagnosis Date of AIDS onset ___/___/___

Details ....

Was this woman on drug treatment when she became pregnant? [ ] No [ ] Yes Started ___/___/___

If Yes, specify drug(s) .... Continuing? [ ] No [ ] Yes

.... Date stopped ___/___/___

Drug treatment changed or started during pregnancy? [ ] Not applicable. Pregnancy not continuing to term

[ ] No [ ] Not yet decided [ ] Drug treatment declined [ ] Yes, changed or started, details below:

Drug(s) .... Date started or

.... due to start ___/___/___

RECENT TEST RESULTS

Viral load .... copies/ml (............. $\log_{10}$) test .... Date ___/___/___

T-cell subsets [ ] not done, or give most recent results below (specify units [ ] 10^9/l [ ] 10^6/l [/mm^3])

CD4______% no.________ CD8______% no.________ Total lymphocytes no. ________ ___/___/___

Form completed by: Name ______________________________ Date ___/___/___

Position ________________ Telephone ________________ Email ________________

PLEASE ADD ANY ADDITIONAL INFORMATION OR COMMENTS OVERLEAF.

Appendix F: Full results tables for analyses undertaken in chapter 6

Table F.1: Odds and adjusted odds for wanting (more) children

Maternal factor		Total (N)	Desire children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
Ethnicity (n=450)	Non-African	126	45 (35.7%)	1.00	-	-	1.00	-	-
	African	324	140 (43.2%)	1.37	0.89-2.09	0.15	1.39	0.77-2.49	0.27
Residence (n=450)	Non-London	166	65 (39.2%)	1.00	-	-	1.00	-	-
	London	324	120 (42.3%)	1.14	0.77-1.68	0.52	0.65	0.35-1.19	0.16
Born in UK (n=450)	No	355	158 (44.5%)	1.00	-	-	-	-	-
	Yes	95	27 (28.4%)	0.50	0.30-0.81	**<0.001**	-	-	-
Years in UK (n=310)	<=5 years	175	75 (42.9%)	1.00	-	-	1.00		
	5+ years	135	63 (46.7%)	1.17	0.74-1.83	0.50	1.41	0.77-2.59	0.27
In a partnership (n=450)	No	217	71 (32.7%)	1.00	-	-	1.00	-	-
	Yes	233	114 (48.9%)	1.96	1.34-2.89	**0.001**	1.97	1.16-3.34	**0.013**
Age at diagnosis (n=415)	<=29	211	91 (43.1%)	1.00	-	-	1.00	-	-
	>29	239	94 (39.3%)	0.85	0.59-1.25	0.41	1.04	0.58-1.88	0.89
Years since diagnosis (n=433)	<=5 years	286	124 (43.4%)	1.00	-	-	1.00	-	-
	5+ years	147	55 (37.4%)	0.78	0.52-1.17	0.24	0.71	0.35-1.44	0.34
Partner HIV status (n=196)[2]	Negative	88	44 (50.0%)	1.00	-	-	-	-	-
	Positive	108	52 (48.1%)	0.93	0.53-1.63	0.80	-	-	-
History of IDU (n=445)	No	410	169 (41.2%)	1.00	-	-	1.00	-	-
	Yes	35	13 (37.1%)	0.84	0.41-1.72	0.64	1.67	0.36-7.76	0.51
Current HIV symptoms (n=433)	None	234	95 (40.6%)	1.00	-	-	-	-	-
	Mild/Mod.	173	74 (42.8%)	1.09	0.73-1.63	0.66	-	-	-
	Severe	26	8 (30.8%)	0.65	0.27-1.55	0.33	-	-	-
CD4 count (n=345)	<350	194	78 (40.2%)	1.00	-	-	-	-	-
	>=350	151	63 (41.7%)	1.06	0.69-1.64	0.78	-	-	-

Table F.1: Odds and adjusted odds for wanting (more) children (contd)

Maternal factor		Total (N)	Desire children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
HIV-related therapy (n=445)	No	141	69 (48.9%)	1.00	-	-	1.00	-	-
	Yes	304	115 (37.8%)	0.63	0.42-0.95	**0.027**	0.88	0.50-1.55	0.66
No. of children (n=450)	<2	254	127 (50.0%)	1.00	-	-	1.00		
	>=2	196	58 (29.6%)	0.42	0.28-0.62	**<0.001**	0.28	0.15-0.51	**<0.001**
Has had a positive child(n=271)	No	210	69 (32.9%)	1.00	-	-	-	-	-
	Yes	61	23 (37.7%)	1.24	0.68-2.24	0.48	-	-	-
Ever had a misc. or TOP (n=450)	No	269	99 (36.8%)	1.00	-	-	1.00		
	Yes	181	86 (47.5%)	1.55	1.06-2.28	**0.024**	1.10	0.65-1.88	0.72
Pregnant at diagnosis (n=450)	No	320	130 (40.6%)	1.00	-	-	-	-	-
	Yes	130	55 (42.3%)	1.07	0.71-1.62	0.74	-	-	-
Trying for a pregnancy (n=336)	No	263	92 (34.9%)	1.00	-	-	1.00	-	-
	Yes	73	53 (72.6%)	4.92	2.77-8.74	**<0.001**	3.46	1.68-7.13	**<0.001**

[1]Adjusted for ethnicity, residence, years in UK, partnership status, age at diagnosis, years since HIV diagnosis, HIV-related therapy, history of injecting drug use, number of previous children, previous miscarriage or termination of pregnancy, trying for a pregnancy >6 months. These were the factors found to be associated with child-bearing in univariate analyses. Whether or not the woman had been born in the UK was not included in the adjusted analysis as this variable was closely correlated to years in the UK.

[2] 37 cases were not known or not tested and therefore not included in the analysis

Table F.2: Odds and Adjusted odds for not wanting children after an HIV diagnosis[1]

Maternal factor		Total (n)	Not want children N (%)	OR	95% CI	P value	Adjusted OR[2]	95% CI	P value
Ethnicity (n=356)	Non-African	90	41 (45.6%)	1.00	-	-	1.00	-	-
	African	266	114 (42.9%)	0.90	0.55-1.45	0.66	2.01	0.78-5.13	0.15
Residence (n=356)	Non-London	123	57 (46.3%)	1.00	-	-	1.00	-	-
	London	233	98 (42.1%)	0.84	0.54-1.30	0.44	0.83	0.40-1.74	0.63
Born in UK (n=356)	No	286	120 (41.9%)	1.00	-	-	-	-	-
	Yes	70	35 (50.0%)	1.38	0.82-2.34	0.23	-	-	-
Years in UK (n=320)	<=5 years	182	85 (46.7%)	1.00	-	-	1.00	-	-
	5+ years	138	57 (41.3%)	1.26	0.71-2.21	0.43	1.29	0.64-2.60	0.48
In a partnership (n=356)	No	178	82 (46.1%)	1.00	-	-	1.00	-	-
	Yes	178	73 (41.0%)	0.81	0.54-1.24	0.34	0.83	0.44-1.56	0.56
Age at diagnosis (n=356)	<=29	157	82 (52.2%)	1.00	-	-	1.00	-	-
	>29	199	73 (36.7%)	0.53	0.35-0.81	**0.003**	0.93	0.47-1.85	0.84
Years since diagnosis (n=341)	<=5 years	224	88 (39.3%)	1.00	-	-	1.00	-	-
	5+ years	117	62 (53.0%)	1.74	1.11-2.74	**0.016**	1.75	0.76-3.99	0.19
Partner HIV status (n=153)	Negative	69	29 (42.0%)	1.00	-	-	-	-	-
	Positive	84	38 (45.2%)	1.14	0.60-2.17	0.69	-	-	-
History of IDU (n=352)	No	329	140 (42.6%)	1.00	-	-	1.00	-	-
	Yes	23	13 (56.5%)	1.76	0.75-4.12	0.20	1.73	0.26-11.77	0.57
Current HIV symptoms (n=341)	None	185	77 (41.6%)	1.00	-	-	-	-	-
	Mild/Mod.	132	64 (48.5%)	1.32	0.84-2.07	0.23	-	-	-
	Severe	24	10 (41.7%)	1.00	0.42-2.37	0.99	-	-	-
CD4 count (n=277)	<350	158	67 (42.2%)	1.00	-	-	-	-	-
	>=350	119	51 (42.9%)	1.02	0.63-1.65	0.94	-	-	-

Table F.2: Odds and Adjusted odds for not wanting children after an HIV diagnosis[1] (contd)

Maternal factor		Total (n)	Not want children N (%)	OR	95% CI	P value	Adjusted OR[2]	95% CI	P value
HIV-related therapy (n=351)	No	102	48 (47.1%)	1.00	-	-	1.00	-	-
	Yes	249	105 (42.2%)	0.82	0.52-1.30	0.40	0.65	0.33-1.29	0.22
No. of children at diagnosis (n=356)	<2	187	98 (52.4%)	1.00	-	-	1.00	-	-
	>=2	169	57 (33.7%)	0.46	0.30-0.71	<0.001	1.46	0.70-3.01	0.31
Has had a positive child(n=222)	No	175	72 (41.1%)	1.00	-	-	-	-	-
	Yes	47	17 (36.2%)	0.81	0.42-1.58	0.54	-	-	-
Ever had a misc. or TOP (n=356)	No	213	88 (41.3%)	1.00	-	-	1.00	-	-
	Yes	143	67 (46.9%)	1.25	0.82-1.92	0.30	1.11	0.59-2.09	0.75
Pregnant at diagnosis (n=356)	No	250	103 (41.2%)	1.00	-	-	-	-	-
	Yes	106	52 (49.1%)	1.37	0.87-2.17	0.17	-	-	-
Trying for a pregnancy (n=356)	No	302	133 (44.0%)	1.00	-	-	1.00	-	-
	Yes	54	22 (40.7%)	0.87	0.49-1.57	0.65	0.61	0.27-1.36	0.23

[1] Comparison of women who did not want children anymore after their diagnosis with women who said HIV had had no effect on their childbearing intentions

[2]Adjusted for ethnicity, residence, years in UK, partnership status, age at diagnosis, years since HIV diagnosis, HIV-related therapy, history of injecting drug use, number of previous children, previous miscarriage or termination of pregnancy, trying for a pregnancy >6 months. These were the factors found to be associated with child-bearing in univariate analyses. Whether or not the woman had been born in the UK was not included in the adjusted analysis as this variable was closely correlated to years in the UK.

Table F.3: Odds and Adjusted odds for changing mind about having children after improvements in HIV-related treatments

Maternal factor		Total (n)	Want children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
Ethnicity (n=144)	Non-African	39	15 (38.5%)	1.00	-	-	1.00	-	-
	African	105	34 (32.4%)	0.63	0.26-1.53	0.31	1.25	0.19-7.85	0.81
Residence (n=144)	Non-London	51	12 (23.5%)	1.00	-	-	1.00	-	-
	London	93	37 (39.8%)	2.06	0.88-4.79	0.095	1.21	0.31-4.75	0.78
Born in UK (n=144)	No	111	39 (35.1%)	1.00	-	-	-	-	-
	Yes	33	10 (30.3%)	1.15	0.43-3.06	0.77	-	-	-
Years in UK (n=135)	<=5 years	81	28 (34.6%)	1.00	-	-	1.00	-	-
	5+ years	54	18 (33.3%)	1.39	0.57-3.38	0.47	0.90	0.26-3.10	0.87
In a partnership (n=144)	No	76	16 (21.1%)	1.00	-	-	1.00	-	-
	Yes	68	33 (48.5%)	2.48	1.11-5.50	**0.026**	8.24	1.87-36.13	**0.005**
Age at diagnosis (n=144)	<=29	74	27 (36.5%)	1.00	-	-	1.00	-	-
	>29	70	22 (31.4%)	0.68	0.31-1.47	0.33	0.94	0.26-3.46	0.93
Years since diagnosis (n=140)	<=5 years	81	26 (32.1%)	1.00	-	-	1.00	-	-
	5+ years	59	22 (37.3%)	1.40	0.63-3.09	0.41	1.15	0.25-5.30	0.85
Partner HIV status (n=63)	Negative	26	13 (50.0%)	1.00	-	-	-	-	-
	Positive	37	18 (48.6%)	0.96	0.32-2.91	0.94	-	-	-
History of IDU (n=140)	No	129	45 (34.9%)	1.00	-	-	1.00	-	-
	Yes	13	3 (23.1%)	0.83	0.18-3.93	0.82	0.27	0.01-9.54	0.47
Current HIV symptoms (n=140)	None	70	31 (44.3%)	1.00	-	-	-	-	-
	Mild/Mod.	60	18 (30.0%)	0.69	0.30-1.57	0.38	-	-	-
	Severe	10	0 (0%)	-	-	-	-	-	-
CD4 count (n=111)	<350	63	22 (34.9%)	1.00	-	-	-	-	-
	>=350	48	13 (27.1%)	0.89	0.36-2.20	0.80	-	-	-

Table F.3: Odds and Adjusted odds for changing mind about having children after improvements in HIV-related treatments (contd)

Maternal factor		Total (n)	Want children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
HIV-related therapy (n=142)	No	41	12 (29.3%)	1.00	-	-	1.00	-	-
	Yes	101	37 (36.6%)	2.02	0.86-4.75	0.11	6.67	1.44-30.80	**0.015**
No. of children at diagnosis(n=144)	<2	87	35 (40.2%)	1.00	-	-	1.00	-	-
	>=2	57	14 (24.6%)	0.56	0.25-1.26	0.16	0.15	0.03-0.65	**0.011**
Has had a positive child(n=86)	No	69	18 (26.1%)	1.00	-	-	-	-	-
	Yes	17	6 (35.3%)	1.61	0.45-5.77	0.46	-	-	-
Ever had a misc. or TOP (n=144)	No	80	28 (35.0%)	1.00	-	-	1.00	-	-
	Yes	64	21 (32.8%)	0.90	0.41-1.96	0.79	0.68	0.21-2.18	0.51
Pregnant at diagnosis (n=144)	No	95	34 (35.8%)	1.00	-	-	-	-	-
	Yes	49	15 (30.6%)	0.77	0.34-1.75	0.54	-	-	-
Trying for a pregnancy (n=144)	No	123	39 (31.7%)	1.00	-	-	1.00	-	-
	Yes	21	10 (47.6%)	2.09	0.70-6.27	0.19	2.38	0.52-10.79	0.26

[1]Adjusted for ethnicity, residence, years in UK, partnership status, age at diagnosis, years since HIV diagnosis, HIV-related therapy, history of injecting drug use, number of previous children, previous miscarriage or termination of pregnancy, trying for a pregnancy >6 months. Whether or not the woman had been born in the UK was not included in the adjusted analysis as this variable was closely correlated to years in the UK.

Table F.4: Odds and adjusted odds for changing mind about having children after improvements in interventions which reduce MTCT

Maternal factor		Total (n)	Want children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
Ethnicity (n=129)	Non-African	38	18 (47.4%)	1.00	-	-	1.00	-	-
	African	91	36 (39.6%)	0.63	0.27-1.47	0.29	1.70	0.28-10.37	0.57
Residence (n=129)	Non-London	47	15 (31.9%)	1.00	-	-	1.00	-	-
	London	82	39 (47.6%)	2.24	1.00-4.99	**0.048**	1.77	0.42-7.44	0.44
Born in UK (n=129)	No	97	38 (39.2%)	1.00	-	-	-	-	-
	Yes	32	16 (50.0%)	1.85	0.75-4.56	0.18	-	-	-
Years in UK (n=122)	<=5 years	74	34 (45.9%)	1.00	-	-	1.00	-	-
	5+ years	48	17 (35.4%)	2.36	0.93-5.99	0.07	1.84	0.54-6.25	0.33
In a partnership (n=129)	No	62	18 (29.0%)	1.00	-	-	1.00	-	-
	Yes	67	36 (53.7%)	2.15	0.99-4.69	0.053	5.34	1.29-22.21	**0.021**
Age at diagnosis (n=129)	<=29	68	33 (48.5%)	1.00	-	-	1.00	-	-
	>29	61	21 (34.4%)	0.64	0.30-1.37	0.25	1.20	0.33-4.38	0.78
Years since diagnosis (n=126)	<=5 years	70	27 (38.6%)	1.00	-	-	1.00	-	-
	5+ years	56	26 (46.4%)	1.54	0.71-3.35	0.28	1.28	0.28-5.81	0.75
Partner HIV status (n=62)	Negative	27	16 (59.3%)	1.00	-	-	-	-	-
	Positive	35	18 (51.4%)	0.60	0.21-1.79	0.36	-	-	-
History of IDU (n=127)	No	115	48 (41.7%)	1.00	-	-	1.00	-	-
	Yes	12	5 (41.7%)	1.27	0.32-5.04	0.73	0.49	0.01-19.63	0.70
Current HIV symptoms (n=127)	None	61	31 (50.8%)	1.00	-	-	-	-	-
	Mild/Moderate	57	22 (38.6%)	0.92	0.41-2.05	0.84	-	-	-
	Severe	9	1 (11.1%)	0.14	0.02-1.24	0.077	-	-	-
CD4 count (n=101)	<350	55	23 (41.8%)	1.00	-	-	-	-	-
	>=350	46	16 (34.8%)	0.90	0.38-2.15	0.82	-	-	-

Table F.4: Odds and adjusted odds for changing mind about having children after improvements in interventions which reduce MTCT (contd)

Maternal factor		Total (n)	Want children N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
HIV-related therapy (n=127)	No	38	17 (44.7%)	1.00	-	-	1.00	-	-
	Yes	89	37 (41.6%)	1.15	0.51-2.59	0.73	3.81	0.86-16.98	0.079
No. of children at diagnosis(n=129)	<2	80	41 (51.3%)	1.00	-	-	1.00	-	-
	>=2	49	13 (26.5%)	0.37	0.16-0.84	**0.017**	0.15	0.03-0.64	**0.010**
Has had a positive child(n=76)	No	61	20 (32.8%)	1.00	-	-	-	-	-
	Yes	15	5 (33.3%)	1.14	0.32-4.10	0.84	-	-	-
Ever had a misc. or TOP (n=129)	No	71	27 (38.0%)	1.00	-	-	1.00	-	-
	Yes	58	27 (46.6%)	1.45	0.68-3.11	0.34	1.09	0.32-3.67	0.14
Pregnant at diagnosis (n=129)	No	82	36 (43.9%)	1.00	-	-	-	-	-
	Yes	47	18 (38.3%)	0.73	0.33-1.59	0.43	-	-	-
Trying for a pregnancy (n=129)	No	108	44 (40.7%)	1.00	-	-	1.00	-	-
	Yes	21	10 (47.6%)	1.52	0.53-4.36	0.43	1.25	0.26-5.90	0.78

[1]Adjusted for ethnicity, residence, years in UK, partnership status, age at diagnosis, years since HIV diagnosis, HIV-related therapy, history of injecting drug use, number of previous children, previous miscarriage or termination of pregnancy, trying for a pregnancy >6 months. Whether or not the woman had been born in the UK was not included in the adjusted analysis as this variable was closely correlated to years in the UK.

Table F.5: Odds and Adjusted odds for having had a pregnancy after HIV diagnosis[2]

Maternal factor		Total (n)	Had pregnancy N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
Ethnicity (n=312)	Non-African	105	24 (22.9%)	1.00	-	-	1.00	-	-
	African	207	47 (22.7%)	0.99	0.57-1.74	0.98	3.93	1.21-12.80	**0.023**
Residence (n=312)	Non-London	100	24 (24.0%)	1.00	-	-	1.00	-	-
	London	212	47 (22.2%)	0.90	0.51-1.58	0.72	1.21	0.41-3.58	0.73
Born in UK (n=312)	No	231	51 (22.1%)	1.00	-	-	-	-	-
	Yes	81	20 (24.7%)	1.16	0.64-2.09	0.63	-	-	-
Years in UK (n=205)	<=5 years	89	18 (20.2%)	1.00	-	-	1.00	-	-
	5+ years	116	30 (25.9%)	1.38	0.71-2.67	0.35	0.95	0.40-2.28	0.91
In a partnership (n=312)	No	150	27 (18.0%)	1.00	-	-	1.00	-	-
	Yes	162	44 (27.2%)	1.69	0.99-2.92	0.06	2.29	1.05-5.01	**0.036**
Age at diagnosis (n=312)	<=29	162	52 (32.1%)	1.00	-	-	1.00	-	-
	>29	150	19 (12.7%)	0.31	0.17-0.55	**<0.001**	0.54	0.23-1.28	0.16
Years since diagnosis (n=295)	<=5 years	148	18 (12.2%)	1.00	-	-	1.00	-	-
	5+ years	147	53 (36.1%)	4.07	2.24-7.39	**<0.001**	4.94	1.91-12.79	**0.001**
Partner HIV status (n=144)	Negative	66	19 (28.8%)	1.00	-	-	-	-	-
	Positive	78	22 (28.2%)	0.97	0.47-2.01	0.94	-	-	-
History of IDU (n=310)	No	277	61 (22.0%)	1.00	-	-	1.00	-	-
	Yes	33	10 (30.3%)	1.54	0.70-3.40	0.29	1.55	0.25-9.67	0.64
Current HIV symptoms (n=303)	None	159	40 (25.2%)	1.00	-	-	-	-	-
	Mild/Mod.	123	25 (20.3%)	0.75	0.43-1.33	0.34	-	-	-
	Severe	21	3 (14.3%)	0.49	0.14-1.77	0.28	-	-	-
CD4 count (n=239)	<350	122	25 (20.5%)	1.00	-	-	-	-	-
	>=350	117	25 (21.4%)	1.05	0.57-1.96	0.87	-	-	-

Table F.5: Odds and Adjusted odds for having had a pregnancy after HIV diagnosis[2] (contd)

Maternal factor		Total (n)	Had pregnancy N (%)	OR	95% CI	P value	Adjusted OR[1]	95% CI	P value
HIV-related therapy (n=308)	No	88	23 (26.1%)	1.00	-	-	1.00	-	-
	Yes	220	46 (20.9%)	0.75	0.42-1.33	0.32	0.76	0.33-1.77	0.53
No. of children at diagnosis(n=312)	<2	221	58 (26.2%)	1.00	-	-	1.00	-	-
	>=2	91	13 (14.3%)	0.47	0.24-0.91	**0.024**	0.48	0.18-1.31	0.15
Has had a positive child(n=202)	No	154	49 (31.8%)	1.00	-	-	-	-	-
	Yes	48	16 (33.3%)	1.07	0.54-2.13	0.84	-	-	-
Ever had a misc. or TOP (n=312)	No	180	38 (21.1%)	1.00	-	-	1.00	-	-
	Yes	132	33 (25.0%)	1.25	0.73-2.12	0.42	0.69	0.31-1.53	0.36
Pregnant at diagnosis (n=312)	No	227	45 (19.8%)	1.00	-	-	-	-	-
	Yes	85	26 (30.6%)	1.78	1.01-3.14	0.05	-	-	-
Trying for a pregnancy (n=312)	No	257	57 (22.2%)	1.00	-	-	1.00	-	-
	Yes	55	14 (25.5%)	1.20	0.61-2.35	0.60	0.60	0.23-1.60	0.31

[1]Adjusted for ethnicity, residence, years in UK, partnership status, age at diagnosis, years since HIV diagnosis, HIV-related therapy, history of injecting drug use, number of previous children, previous miscarriage of termination or pregnancy, trying for a pregnancy >6 months. Whether or not the woman had been born in the UK was not included in the adjusted analysis as this variable was closely correlated to years in the UK.

[2] Analysis restricted to women who had been diagnosed with HIV for at least 2 years

Appendix G: Full result tables for analyses undertaken in chapter 7

Table G.1: Numbers of infections in women at risk of pregnancy in Great Britain

				1997	2000	2001	2002
Diagnosed	**London**	**Women born in SSA**	**<2 children**	580	1820	2100	2770
Diagnosed	**London**	**Women born in SSA**	**>=2 children**	100	320	380	480
Diagnosed	**London**	**Other**	**<2 children**	610	930	1210	1170
Diagnosed	**London**	**Other**	**>=2 children**	80	120	160	160
Diagnosed	**Rest GB**	**Women born in SSA**	**<2 children**	140	1060	990	1360
Diagnosed	**Rest GB**	**Women born in SSA**	**>=2 children**	30	220	210	290
Diagnosed	**Rest GB**	**Other**	**<2 children**	420	780	900	1140
Diagnosed	**Rest GB**	**Other**	**>=2 children**	70	140	170	210
Undiagnosed	**London**	**Women born in SSA**	**<2 children**	910	990	1140	1000
Undiagnosed	**London**	**Women born in SSA**	**>=2 children**	390	420	490	430
Undiagnosed	**London**	**Other**	**<2 children**	290	320	420	400
Undiagnosed	**London**	**Other**	**>=2 children**	130	140	180	180
Undiagnosed	**Rest GB**	**Women born in SSA**	**<2 children**	350	580	540	740
Undiagnosed	**Rest GB**	**Women born in SSA**	**>=2 children**	150	250	230	320
Undiagnosed	**Rest GB**	**Other**	**<2 children**	560	730	840	1060
Undiagnosed	**Rest GB**	**Other**	**>=2 children**	240	310	360	460
Total				**5050**	**9130**	**10,320**	**12,170**

able G.2: Table: Numbers of infections in women not at risk of pregnancy in Great Britain

				1997	2000	2001	2002
Diagnosed	London	Women born in SSA	>=45	40	160	260	370
Diagnosed	London	Other	>=45	60	120	160	200
Diagnosed	Rest	Women born in SSA	>=45	20	60	110	170
Diagnosed	Rest	Other	>=45	90	170	200	220
Undiagnosed	London	Women born in SSA	>=45	180	220	340	440
Undiagnosed	London	Other	>=45	90	140	180	230
Undiagnosed	Rest	Women born in SSA	>=45	80	70	130	200
Undiagnosed	Rest	Other	>=45	280	360	430	470
Diagnosed	London	Women born in SSA	Completed family	180	350	460	570
Diagnosed	London	Other	Completed family	80	110	120	120
Diagnosed	Rest	Women born in SSA	Completed family	30	110	180	330
Diagnosed	Rest	Other	Completed family	80	120	130	160
Diagnosed	London	Women born in SSA	Didn't want children	20	40	50	60
Diagnosed	London	Other	Didn't want children	30	40	40	40
Diagnosed	Rest	Women born in SSA	Didn't want children	10	10	20	30
Diagnosed	Rest	Other	Didn't want children	20	50	60	60
Undiagnosed	London	Women born in SSA	Didn't want children	80	50	40	70
Undiagnosed	London	Other	Didn't want children	50	40	50	50
Undiagnosed	Rest	Women born in SSA	Didn't want children	20	10	30	40
Undiagnosed	Rest	Other	Didn't want children	90	100	110	120
Total				**1530**	**2330**	**3100**	**3950**

Figure G.1: Working example of how HIV estimates for Table 7.4 were generated.: Women born in SSA and resident in London: 2002

The following example shows how data in Table 7.4 were generated, using women born in SSA and resident in London (2002) as the specific example. Diagnosed and undiagnosed estimates were generated for the 2 components of the model separately and finally summed together.

The number of women at risk of pregnancy (component 1) was estimated according to Figure G.1 (as explained on pages 177-179). The overall neonatal seroprevalence (as estimated from table 7.1) was adjusted according to whether or not the woman's infection was diagnosed, the proportion of women who did not want a child after their HIV diagnosis, the number of children the woman had had at time of diagnosis and a fertility differential (Figure G.1). Each prevalence was then applied to the total population of women born in SSA and resident in London to derive the total number of HIV infections. The number of infections estimated was 4680, of which 3250 were diagnosed and 1430 undiagnosed.

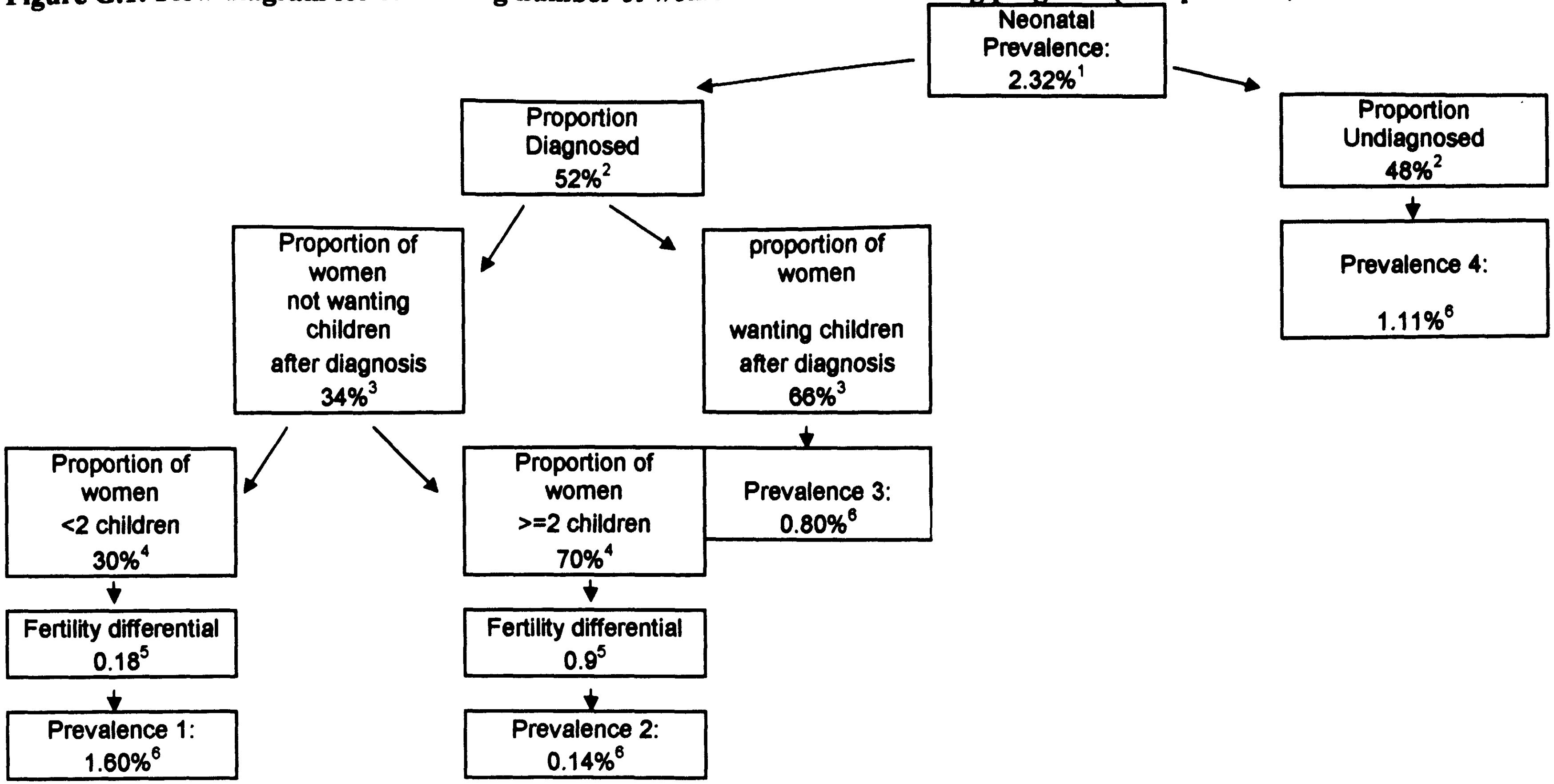
The number of women not at risk of becoming pregnant (component 2) was estimated by the sum of parameters A-E (Table G.3). More details were provided on page 179-181.

Table G.3: Number of women not at risk of being pregnant

	Parameter	Source of data	Sum of infections
A	No. of diagnosed women>45	SOPHID data	370
B	No. of undiagnosed women>45	Estimated using SOPHID data and proportions of infections undiagnosed (table 7.2)	440
C	No. of women who had completed family at time of diagnosis	Questionnaire data. Which showed 17% of women had completed family at diagnosis. This proportion applied to SOPHID women 15-44	570
D	No. of diagnosed women who never wanted children regardless of HIV	Questionnaire data. Which showed 1.8% of women never wanted children. This proportion applied to SOPHID women 15-44	60
E	No. of undiagnosed women who never wanted children regardless of HIV	Estimated using parameter D and proportion of infections undiagnosed (Table 7.2)	70
Total			**1510**

The number of infections for component 2 was estimated at 1510, of which 1000 were diagnosed and 510 undiagnosed. **Therefore combining the data from the 2 components it was estimated there were a total of 6190 infections (4250 diagnosed and 1940 undiagnosed). These data were presented in Table 7.4.**

Figure G.1: Flow diagram for estimating number of women at risk of becoming pregnant (Component 1)



[1] neonatal seroprevalence derived from unlinked anonymous surveys (Ref Table 7.1) [2] Fertility amongst HIV positive women depends on whether the infection was diagnosed or undiagnosed. This data was obtained from Table 7.2 [3] A reduced fertility differential was applied to women who stated in the questionnaire survey that they did not want children anymore after their HIV diagnosis (ref table 6.4) [4] A fertility differential was estimated separately for women who had <2 children and women who had >=2 children at time of diagnosis. The proportions of women in these two categories was estimated using questionnaire data and validated using routine reports of HIV infection amongst women which collect parity data. [5] The estimated fertility differential (Table 7.3) [6] Prevalence rate applied to total population of women born in SSA and resident in London(n=128,670) to generate numbers of infections